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ORIGINAL COMMUNICATIONS.

THE PATHOGENESIS OF SECONDARY TUMORS.

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(Concluded from page 809.)

CHAPTER V.

THE FATE AND MICROSCOPIC STRUCTURE OF PERIOSTEUM AND OTHER PARTICLES OF NORMAL TISSUES EXPERIMENTALLY TRANSPLANTED.

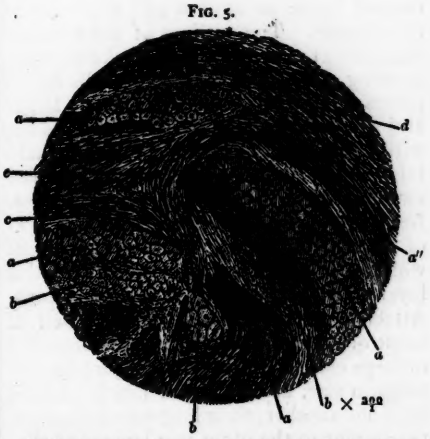
THE gradual development of the periosteal embolus inroduced into the lung of dogs by means of the jugular vein can be perfectly studied, as my preparations represent the different stages. In all the experiments I was careful to take periosteum only, and not to take any bone-structure with it; so that, while removing a fragment of periosteum from the bone, I occasionally examined a similar fragment as to its histological structure, and found it to present appearances which may be thus briefly described. It was composed of two layers,—an outer or fibrous layer, composed of dense fibrous connective tissue, and an inner or so-called osteogenetic layer, made up of areolar connective tissue, rich in cellular elements, also containing some yellow elastic fibres. Both layers were freely supplied with blood-vessels, which carried the blood to and from the bone.

Before introducing the periosteum, I took particular pains to squeeze it, so as to free the blood-vessels from clotted blood, in order that, when the embolus finally became lodged in some vessel, the blood might gain access to the interior of the embolus, and in this way give good support and nutrition.

The fate of the embolus was to get lodged in some branch of the pulmonary artery, just as in the case of the tumor emboli. Here, as there, the embolus produced thrombosis; and, if examined a few days after its introduction, it showed itself to be intimately enveloped by a blood-clot, indicating a tendency towards organization. In sections made still later, the organization of this blood-clot demonstrated the higher phases of organization analogous to those seen in ligation of arteries.*

In experiments of fourteen days after preparing the specimens, a section, stained in carmine and mounted in Canada balsam, presented the following appearance. The artery is seen in transverse section, and exhibits slight evidences of inflammatory change, the adventitia being thickened and filled with proliferating cells; the media appears normal, while the intima of the vessel shows distinct thickening, also due to proliferation of its cells. In the lumen is seen the periosteum folded up and twisted, and in the interspaces formed by the folds of the periosteum and the walls of the blood-vessels are seen masses of an organizing blood-clot, which in some places are beginning to be absorbed. This organizing blood-clot evidently serves as a matrix for the embolus, the latter being dependent temporarily to a great extent upon the clot for its nourishment. The clot is always in direct communication with the intima, and is in turn nourished by the vasa vasorum of the mother vessel. Only in rare instances is the periosteum seen in contact with, and deriving its nourishment directly from, the vasa vasorum.

FIG. 5.



Ossification of periosteal embolus in lung of dog, showing details of the ossifying process. (Experiment No. 34, of 14 days' duration. Drawing reduced to one-fourth of actual size.) *a*. Inner layer of periosteum changed into osteoid tissue. *a'*. Unchanged periosteum. *a''*. Outer layer of periosteum. *b*. Osteoblasts. *c*. Organized thrombus tissue filling interspaces. *d*. Wall of mother vessel in intimate union with embolus. *e*. Band of tissue leading vasa vasorum of mother vessel to the centre of the embolus.

* I would even suggest to those who make studies of the healing of arteries to extend their experimentation to similar artificially-produced emboliems of lung.

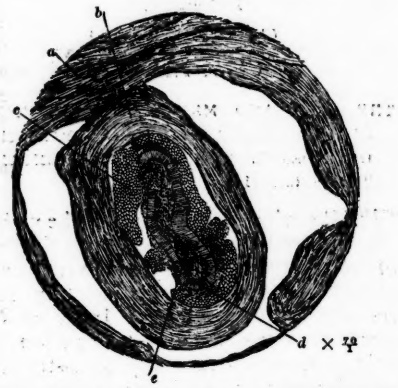
At this place the intercommunication of blood-vessels between the embolus and the wall of the blood-vessel is distinctly seen. The outer layer of the lamella of periosteum, as seen in transverse section, is unchanged. The inner layer shows the beginning of ossification analogous to that seen in fœtal intermembranous bone-formation. At this stage the inner periosteal layer is seen transformed into hyaline glassy cells, very imperfectly stained, and resembling most perfectly the tissue of callus which is produced during the process of healing of bones. This I will call *osteoid tissue*, designated by authors as the osteogenetic layer. It extends as a uniform belt parallel to and bordering the outer layer of the periosteum. The inmost layer of this osteoid belt is made up of large cells, which in some places are seen distinctly to have undergone calcification.

Some preparations made from experiments of the same duration show a somewhat further development of the changes above detailed. Preparations from another of these fourteen days' experiments present the following appearances. The belt of osteoid tissue presents a still more glassy appearance. The outlines of the cells are less distinct, and still did not take carmine staining. The lowest layer of cells has in places unevenly proliferated, forming larger and smaller heaps of cells of osteoid tissue, with distinct calcification; but in the main it continues as a belt, and twists in a curved manner, describing an imperfect ellipse. Next to the osteoid tissue is seen a layer of cells of embryonic character, many of which are distinctly giant-cells, and this layer also is calcified in some portions. Attached to this layer is a third belt of tissue of very uniform width, and composed of large elongated rod-like cells or plates of uniform size, and arranged nearly parallel with one another, their long axes being perpendicular to the other two layers, so that it presents an appearance similar to that of a lining made up of large columnar cells. This layer and the cells composing it correspond precisely, and have the appearance of what are described as osteoblasts. Within this last belt is a long, narrow space, which is filled with lymphoid cells, osteoclasts, etc., forming the elements of marrow of bone. This collection of cells is freely pierced by blood-vessels.

Outside of this ossifying ellipse is seen the organizing clot upon which the embolus depends for some nourishment. But much of this clot is absorbed, yet enough is left to form a capsular fibrinous mass, being attached on the outside to the intima of the blood-vessel.

It will be noticed that true, fully-developed bone is not seen at this stage.

FIG. 6.



Transverse section of a pulmonary arteriole partly filled with organized blood-clot, enclosing a periosteal embolus, which shows the process of ossification, somewhat diagrammatic. (Drawing reduced to one-third.) *a*. Thickened intima (the other coats of the vessel-wall are not represented). *b*. Clot containing the embolus. *c*. Osteoid tissue. *d*. Layer of columnar osteoblasts. *e*. Marrow-cavity filled with young cells.

In experiments of nineteen days' duration the formation of true adult bone is beginning to become prominent. A lamella of bone substitutes the belt of osteoblasts described above, and the interior of the ossifying embolus is largely composed of embryonal marrow-cells and calcifying cell-masses.

In preparations from experiments of thirty-three days' duration extensive ossification is seen. The whole periphery of the embolus represents solid, typical bone-tissue with lamellæ, Haversian canals, and bone corpuscles. In the interior of the embolus the development is not completed, and small islands of marrow and calcified masses are yet demonstrable. The outer layer of the original periosteum is seen upon the periphery.

Experiment of forty-five days' duration shows complete ossification of the embolus; only a few angular marrow-spaces are seen in the interior. The growth and further progressive development of the ossifying embolus are evidently accomplished by apposition,—*i.e.*, by superaddition of bone lamellæ. This is seen from the fact that the embolus assumes bulging outlines, and

occasionally forms projections of bone-tissue.

In experiment of fifty-six days' duration growth continued. The structure of the embolus answers all the requirements of fully-developed bone. Appositional centres are superadded at the periphery, so that the nodular appearance of the embolus is very conspicuous.

Specimens from experiments of seventy days' duration show beautiful and perfect bone-structure. In the foregoing experiments marrow-cavities were always present, but they became smaller in each successive experiment. Here they are altogether obliterated, leaving only spaces for minute Haversian canals.

Preparations from later experiment continue to present the same general appearances, showing only an increase in bulk. One peculiarity, however, is prominent,—*i.e.*, that the Haversian canals become progressively smaller. Thus the bone is very similar to the so-called *ivory-like* (*eburnated*) bone.

Specimens from experiments of one hundred days' duration show that the embolus has reached at least fifty times its original bulk, and, as in all the later experiments, shows extensive proliferation in all directions.

(I omitted to state the important fact that in most of the later experiments the blood-vessel wall and even the fibrous capsule surrounding the embolus were found to have been completely absorbed, so that the bony node appeared bare in the midst of the somewhat compressed lung-tissue.)

In experiment of one hundred days' duration, five small independent centres of ossification were found scattered in different parts of the lobe, which contained the main embolus. This latter was found in a branch of the pulmonary artery, which came off near the base of the lobe, so that it is very possible that fragments became detached and gave rise to these secondary nodules.

Here I would like to interpret properly the appearance of many apparently independent collateral centres of ossification in the immediate neighborhood of the main embolus. These centres may be noticed in close proximity with the main centre. By careful study of successive sections of the embolus the reason of this was obtained. It was seen that these centres did have a connection with the main embolus, each being connected by an isthmus. The isthmus is irregular, curving in different directions, so that in a section of the embolus this connection may not be seen, on account of the curve in the isthmus not being reached by the section-knife. The centres thus appear independent. I will refer to this again in a later chapter. (See Figs. 7 and 8.)

FIG. 7.

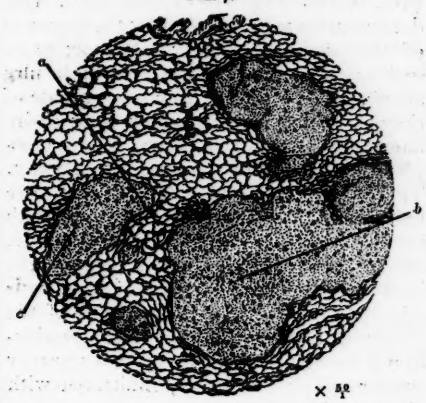
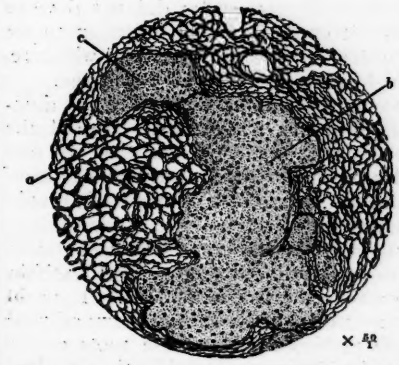


FIG. 8.



Two microscopic sections made from different levels of one of the periosteal emboli developed into bone in lung of dog. (Experiment No. 6, of 100 days' duration. Drawing reduced to one-third of its size.) *a* in Fig. 7 shows connection, *a* in Fig. 8, *dis*connection, of apparently independent centre of ossification *c*. *b*. Main embolus.

Before presenting my conclusion to this chapter I would like to enumerate the details of three other experiments, two of which were performed with adult tissue other than periosteum.

In experiment of thirty-six days' duration, periosteum was introduced into the anterior chamber of the eye of a dog. On making transverse section of the cornea,—*i.e.*, section in the direction of the visual

axis,—preparations were obtained which showed the cornea, a part of the iris, and the capsule of the lens intact. The space between the lens and the cornea was seen filled by a new-formed material. In examining this latter there was seen on one side the periosteal fragment surrounded by a dense fibrous capsule, which, although showing increase in bulk and cellular proliferation, exhibited signs of degeneration. This degeneration was indicated by the presence of the products of fatty metamorphosis, such as compound granule-cells, molecular *dèbris*, etc. Starting from the capsule of the periosteum was seen a new form of inflammatory organized tissue, filling completely the space of the anterior chamber. This tissue was connected by intimate union with the cornea anteriorly, and with the iris and capsule of the lens posteriorly. In fact, this intimate union suggests the idea that the new formation may have taken its origin from the surfaces of the structures mentioned. On close examination it proved to be made up of a vascular areolar connective tissue, infiltrated with pigmented leucocytes.

The outcome of this experiment is that, although the periosteum did not develop itself, it excited enough irritation to set up a slow chronic inflammation, which resulted in the formation of new tissue.

In experiment of fifty-one days' duration, skin was transplanted. In all the specimens it is clearly seen that the embolus became encysted, and attached itself to the wall of the cyst by means of the subcutaneous connective tissue, while the epithelium of the epidermis remained free in some parts and did not connect itself in any way to the wall of the cyst. The subcutaneous connective tissue shows adipose tissue particularly below the roots of the hairs, looking very much like the so-called "columnæ adiposæ." This is the more striking, since before inserting the embolus care was taken to remove most of the subcutaneous connective tissue. The wall of the cyst, which completely encapsules the embolus, is composed of connective tissue, and shows plainly that it has taken its development from the endothelium of the intima. The embolus having been taken from the skin of a black dog, there is to be seen some pigment in the rete mucosum. The hairs are likewise deeply pigmented. Some of the hairs seem to be slightly atrophied and disconnected from their follicles. Pigmented cells are also seen investing the fat-vesicles.

The third experiment to which I have reference is that of transplantation of smooth muscular tissue, taken from a fragment of cervix uteri, removed by Dr. William Goodell, at the University Hospital clinic. (See experiment No. 37 in the table.)

The muscular tissue was examined before introduction, and found to consist of perfectly normal unstriated muscular tissue, and, before introduction, was well squeezed, to rid the blood-vessels of any clots of blood.

As seen from the record in the table, the transplantation was a success. After the lapse of forty-two days the embolus was found of increased bulk, and did not show the slightest retrograde change. As can be distinctly seen in the specimen, the increase in bulk was not in this or any other case due to the presence or superaddition of the organized blood-clot alone, but to an active proliferation of the cells of the transplanted tissue itself. In the embolus under consideration, besides proliferation of the muscular cells, evident from the young cells between the muscular bundles, micrometric measurement reveals increase of the cells.

To the above I may add that the embolus was encapsuled and united with the intima of the blood-vessel in the same manner as described in other successful experiments.

One point may be mentioned before concluding this chapter; it is this: as already stated, I met with many failures in this work of transplantation, a number of which I did not put on record. Yet, after hitting upon proper methods, as detailed in Chapter I., and becoming accustomed by exercise to carry out properly the details of the procedure, I rarely failed. Thus, in experimenting with muscular tissue, I made but one experiment, and this was positive.

It is a matter of regret to me that I cannot present experiments extending over periods of years rather than months. But, such as they are, they are perfectly satisfactory to me. They have fully established definite laws in the growth and development of transplanted tissues. There is not the slightest reason to suppose that this growth and development should be opposed or hindered. On the contrary, I

have full right to conclude that those emboli of normal tissue of periosteum, skin, unstriated muscle-fibres, would, if let alone, have continued to grow, it may be, indefinitely, not having been bound to limits of any physiological purpose as in regeneration. They would have developed into larger tumor-masses. This is the more probable as at no time in the more successful experiments were there any evidences of retrograde changes.

I have also shown that the mode of growth of the emboli of normal tissue was precisely identical with that which I have demonstrated in my experiments with cancer. Conditions, mode of growth, and ultimate results being the same, it naturally follows here, as there, that the development is not due to any specific property of the cells, but is due to the simple vital property of ordinary cell-proliferation.

CHAPTER VI.

REFUTATION OF COHNHEIM'S EMBRYONAL THEORY.

The teachings of Cohnheim on the subject of "Etiology of Tumors" are tersely formulated in the following proposition: "A tumor is the result of a fault or irregularity in the primitive germ."* By this is meant that in embryonic life, during the period when the tissues are forming out of the cellular material, there is some irregularity in the distribution of this material, by which more cells are set apart for a certain tissue or organ than are needed, and that these cells lie dormant until certain conditions, which are yet problematic, stimulate them to growth.

In support of this theory he brings forward the fact of their hereditary and congenital character, conceding, however, that, according to his theory, it is not necessary that the tumor be always born with the person, but only a predisposition thereto is necessary, which predisposition he regards as a superfluous amount of cells situated in the midst of a tissue, and these cells, by virtue of their embryonic nature, have in them potentially the power of proliferation.

He contends that every child may bring with it into the world the cell-material out of which subsequently a tumor may develop; furthermore, that these superfluous cells may be prevented from proliferating by a *physiological opposition* of the surrounding normal tissues;† but, given a disturbance or destruction of this physiological opposition, a tumor will result. Cohnheim even suggests the probability of many persons dying in whom these superfluous cells existed, but certain unknown conditions, together with a strict physiological opposition, prevented their proliferation.‡

On the other hand, one of the conditions that favor their growth is an increased blood-supply to the part, and this is always met with in the active growth of childhood, the period of puberty, menstruation, or pregnancy. Thus it is easily seen how a relation can exist between the different periods of life and the appearance of new formations,—*e.g.*, tumors of the skin and bones, age of puberty; tumors of the genital organs, time of menstruation and pregnancy.

By means of his theory Cohnheim also explains the peculiarity of tumors as regards their appearance in certain localities. It is a well-known fact that we have new formations at the different orifices where there was a stopping or a union of different blastodermic membranes, as in the rectum, stomach, and uterus.§ Here are favorite seats for new formations, and in these places, according to him, are these superfluous cells especially deposited. Where we have an osteoma in the lung, it is due to a development of cartilage-cells left over from the bronchial plates.‖

Thus the germs of every tumor are to be sought for away back in fœtal life, and it is therefore to be regarded as a monstrosity; and, as a monstrosity is explained by some disturbance in the primitive germs of the embryo, he maintains that a tumor should also be thus explained.

I have thus far endeavored to present a brief outline of Cohnheim's embryonal theory, together with its application. As is seen, the essence of the theory consists in regarding a tumor as the result of a proliferation of superfluous misplaced (heterotopic) cells, particular stress being laid upon the supposition that these cells are of embryonic character. Impressed with this idea, a number of Cohnheim's followers undertook extensive experiments, and

* Cohnheim's Allgemeine Pathologie, Berlin, 1877, p. 635.

† *Ibid.*, p. 661. ‡ *Ibid.*, p. 639. § *Ibid.*, p. 641.
‖ *Ibid.*, p. 644.

the results of their experimentation seemed to furnish an anatomical basis for Cohnheim's theory. The most successful of these experiments seem to be those of Leopold, whose results I will quote immediately. I would like, however, to state that several years previous to Leopold, Zahn made experiments, and obtained results essentially identical with those of Leopold. It also appears that Zahn was in no way influenced by Cohnheim's ideas. Leopold, who worked under the direct supervision of Cohnheim, experimented with the following tissues. He transplanted both fœtal and adult tissues into the anterior chamber of the eye, jugular vein, and abdominal cavity of rabbits. The tissues used were cartilage, bone, skin with hair, intestine, whole extremities with and without hair and nails, whole heart, large pieces of rib, and whole fœtal head. From five series of experiments, he draws the following conclusions:

"Transplanted cartilage from adult rabbits is absorbed, or remains in very exceptional cases stationary.

"Transplanted cartilage from fœtal living rabbits continues to grow every time, so that it may become two or three hundred times the size of the particles transplanted, thus giving rise to true tumors." These tumors he calls *enchondromata*.

The experimenter describes the mode of development and ultimate fate of each transplanted tissue. In the case of transplanted cartilage, he speaks of the formation of bone with marrow-cavities, etc. A tumor presenting these characteristics he calls an *enchondroma*.

Surely this is not in accordance with standard pathological terminology. A calcified mass of tissue with marrow-cavities would ordinarily pass for bone, and a tumor with such characteristics would properly be called an osteoma. However, his experiments show that embryonic tissues possess eminently the power of proliferation, and that adult tissues only in exceptional cases keep from being absorbed; but my experiments clearly show that adult tissue may also continue to grow,—that periosteum introduced into the jugular vein of a dog will proliferate and form small, bony tumor-masses in the lungs. This is entirely at variance with the results obtained by Cohnheim and Maas,—namely, that adult tissue (periosteum) transplanted became absorbed after twenty days.

Since the publication of the results of my experiments by Dr. H. F. Formad, who read a paper on "The Etiology of Tumors" before the Philadelphia Pathological Society, April 28, 1881, in which he embodied the results of some of my experiments, there have appeared two other papers, which to a great extent confirm my observation.

Prudden experimented with adult hyaline cartilage taken from the head of the femur of a rabbit, transplanting the same into the subcutaneous tissue of other rabbits, and in one case there was an actual new formation of hyaline cartilage. The conclusions which he draws from his experiments are as follows: "That in a rabbit the cells of bits of cartilage transplanted alive may live unchanged for many months, or may lead to the new formation of embryonal cartilage, which may undergo active proliferation."

Ollier, of Lyons, describes a case of successful transplantation of bone, and one of his conclusions is that "transplanted bone is capable of living and growing." What interests me in Ollier's operation is the fact that the transplanted adult tissue was not absorbed, thus confirming my observation that transplanted adult tissues do not disappear. In this respect his experiments have a direct bearing upon this subject; still, the ultimate results are not pertinent here, as they refer more to the subject of regeneration.

Thus transplanted adult tissue may continue to grow as well as embryonic tissue, and whatever embryonic cells are potentially able to do lies in the power of any living adult cellular tissue. It is one of the grand principles of modern cellular pathology that all new formations arise from pre-existing cellular elements; and, as the cells of every new formation have their prototype in the living mature organism, it is not unreasonable to suppose that these cells may be the germs of a neoplasm. To say that they arise from embryonal cells alone only removes the problem farther back. The question naturally suggests itself, Where do these embryonal cells come from? Under what conditions are they deposited?—which of course can never be determined. A subject is not explained by putting it beyond our reach: such a treatment merely augments its inexplicableness.

The experiments of Cohnheim and Maas

(recorded in *Virchow's Archiv*, vol. lxxix.) are incorrect. They must have been conducted carelessly, as their results could not be confirmed. Cohnheim and Maas failed to transplant periosteum successfully, and they explained their failure upon the ground that the transplanted tissue was not of embryonal character.

I repeated their experiments, and out of a series of thirty-eight found that in sixteen the periosteum continued to develop and did not disappear. I have shown also that adult muscular tissue and skin grew vigorously when transplanted into the lungs. (See Chapter IV.)

And now that it has been proved that adult tissues grow as well as embryonal tissues, the whole theory of the embryonal-tumor development is altogether fallacious, if it must depend for its support upon such results as were derived from the experiments in this direction of Cohnheim and Maas and of Leopold.

CHAPTER VII.

APPLICATION OF RESULTS OBTAINED FROM THE EXPERIMENTS TO METASTASIS AND SECONDARY TUMORS.

The experiments which I have performed and tabulated show that a particle of adult tissue, if dislodged from the parent mass and carried off by the circulation, may continue to grow and increase in size. The periosteal embolus gets lodged in a vessel too small to admit its passage, and, the circulation in it being maintained, as in a thrombus, by means of the vasa vasorum, it ossifies.

These experiments were repeated after the method of Cohnheim and Maas, but with different results: whereas in my experiments the embolus was found, after the lapse of one hundred days, projecting from the surface of the lung, in the experiments of Cohnheim and Maas, after twenty days, the embolus could no longer be felt externally, but was found, a shrunken mass, without ossification, within the blood-vessel, and after thirty days all trace of it disappeared.

Therefore, having found the embolus after one hundred days increased in size and in a healthy condition,—*i.e.*, without any trace of degeneration,—there can be no doubt that such an embolus may continue to grow indefinitely, and form an abnormal mass of tissue,—a tumor.

The analogy between the process just described and that of metastasis of tumors is very close, and the idea that the embolic process underlies metastasis is by no means new.

By metastasis of tumors we understand the carrying of particles of living tissue through the system by means of the blood-vessels or lymphatics. Pathologists define it as that process by which morbid changes are transferred from one primary diseased part or condition of the body to another.

As to the fact of metastasis there is or can be no doubt or dispute, but as to the explanation of the fact there exists the greatest diversity of opinion.

The humoral pathologic school hold that the cause of secondary tumors is the same as that which produces the primary ones, namely, a dyscrasia, or peculiar unknown diseased condition of the blood or blood-making apparatus. This theory is maintained by Billroth, in his Surgical Pathology, where he compares the diathesis of tumor-formation to the scrofulous and tuberculous diathesis. In support of this theory many facts are presented, chief among which is this: that after a tumor has been removed from one part of the body, years later, it may be, a secondary tumor of the same structure as the primary one will develop in some internal organ. The secondary lesion, according to this theory, is secondary only in point of time, and has no relation with the primary tumor further than that it is the issue of a common cause,—dyscrasia of the blood. Thus the relation is one of time, and in no way anatomical.

This view—once held by the majority of leading pathologists—is now generally discarded, and most conclusive proof against it appears to me in the complete failure to produce tumors when tumor-juices free from tumor-particles were injected.

The process is now regarded as resting upon an anatomical basis, and the secondary tumors are believed to be the result of the development of tumor-emboli. The question of dispute here is whether the emboli infect the surrounding tissue by a species of metabolism, and thus give rise to secondary tumors, or whether they grow centrally and produce tumors by virtue of inherent cell-proliferation. Upon this

point I would offer the following: in my experiments with tumor-particles the particle transplanted never produced any changes in the surrounding tissue indicating any infection, but, on the contrary, it grew independently if it grew at all. In favor of a central growth of the embolus is also the shape of metastatic deposits. It is generally a known fact, among those who investigate this matter closely, that all secondary tumors grow as nodes, and never at the expense of the surrounding tissue.*

One of the strongest points in favor of an infection or transformation of the surrounding tissue was the observation that, in cancer, around the principal tumor-mass in the surrounding connective tissue there existed scattered and isolated cancer-nests. These were composed of epithelial cells, and were observed to have no connection with the main tumor. It was therefore inferred that a peculiar power of transformation emanated from the primary cancer which transformed the surrounding connective tissue into epithelioid elements.

But it has been discovered by Waldeyer and Pagenstecher† that the epithelial cells from a freshly-extirpated cancer possess the power of amœboid motion. This was supposed to explain fully the appearance of these isolated groups of epithelial cells. Yet these isolated epithelial cancer-nests can be explained in a much more plausible manner, so that the amœboid motion of the cells is not at all necessary.

It is a well-known fact that the proliferation of cancer-growths follows the lymph-channels of the connective tissue. These lymph-channels run by no means in a straight direction, but travel in the most circuitous routes. For instance, a channel may start from a primary focus of cell-proliferation, describe a curve, and again reach the level of the primary focus, at the same time the distal end of the curve being some distance from the starting-point. Under such circumstances, a section made across the growth in a straight direction shows isolated cancer-foci, which are nothing more than the distal ends of the curving lymph-channels filled with cancer-cells. Of this fact I have convinced myself by an investigation of the mode of growth of my periosteal emboli in the lungs, which presented similar appearances in microscopic sections. I frequently saw isolated centres of ossification which I was unable to explain until by careful examination of successive sections I discovered that they were nothing more than transverse sections of extended, curved prolongations from the main or central ossifying embolus. (See Figs. 7 and 8.)

Some of the propositions and views referred to in the different chapters of my paper have been suggested and spoken of properly by various observers, but only on mere hypothetical grounds. I feel happy that I succeeded in my research in furnishing facts and proofs by experiments which appear to give a more firm basis for the explanation of the origin and nature of secondary tumors, and which I trust will help to remove this question from the domain of mere speculation.

In my original manuscript (deposited in the Stillé Library of the University of Pennsylvania) I have embodied twenty-five micro-photographs, taken from my specimens, which prove and demonstrate well all the points brought forward. The high price of printing photographs induced me to limit myself, however, to but a few cuts (accurate copies from the photographs) inserted in this paper.

UNIVERSITY OF PENNSYLVANIA, February, 1882.

* In favor of the embolic origin of secondary growths is their nearly exclusive peripheral location in organs, and also the fact that experimentally-produced emboli have a similar location.

† Birch-Hirschfeld, Patholog. Anatomie, 1877, p. 118.

VIRULENCE OF NORMAL HUMAN SALIVA.

BY GEORGE M. STERNBERG,
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IN the *Medical Times* of June 17, pp. 627–631, is an interesting paper by Dr. Charles Claxton, giving the results of a series of experiments "performed in great part as a check upon those of Sternberg."

The results reported confirm in the most essential particulars those which I had previously obtained, and the main object of the present communication is to say that I believe that Dr. Claxton is quite right in supposing that the dark pigment often found in the spleens of rabbits dead from this form of septæmia "*is due to post-mortem change.*"

I suspected as much at the time I made my report, but refrained from saying so, inasmuch as I was not quite sure of it, and hoped to make further observations with

reference to this point. I therefore contented myself with mentioning the fact of the presence of this dark-colored pigment. My belief that this pigment in the spleens of septæmic rabbits is identical *in appearance* with that found in the spleens of malarial-fever patients is based upon a comparison with mounted specimens of the latter, exhibited to me by Dr. Formad at the time I was conducting my experiments, with his kind assistance, in Philadelphia. We both agreed that the pigment supposed to be characteristic of malarial fever resembled exactly the pigment found in the spleens of these septæmic rabbits.

The possibility that the dark pigment found in the spleen, etc., of malarial-fever patients is likewise due to post-mortem change has also occurred to me, but I have hesitated to raise a question of this kind with reference to a matter which is so generally accepted as well settled by the researches of leading pathologists in various parts of the world.

This change in the spleens of septæmic rabbits, if post-mortem, is not necessarily a putrefactive change; indeed, I am rather inclined to believe that it is due to the chemical action of some fluid which escapes in small quantity from some of the viscera into the cavity of the abdomen. I infer this from the fact that dependent portions of the spleen are most discolored and contain the dark pigment in the greatest quantity, and from the further fact that spleens not pigmented do not become so, according to my observation, after they are removed from the body of the animal. That post-mortem changes have frequently been mistaken by pathologists for the results of pathological processes can scarcely be doubted; and when we consider how promptly such changes occur in hot climates, and especially after death from septic diseases, this is not surprising.

If it is true that the black pigment sometimes found in the spleens of septæmic rabbits is due to post-mortem change, then it is also true that *this change may occur within twelve hours during the month of January in the latitude of Philadelphia;* for my post-mortem examinations were all made within this time, and in a certain number of cases the black pigment was present, a fact verified by my friend Dr. Formad. In pursuing these experiments I have always endeavored to make my post-mortem examinations as promptly as possible, but, as the rabbits very commonly die during the night, the earliest practicable time has generally been in the morning, immediately upon commencing work in the laboratory. Sometimes the victims are found in the death-struggle,—as noted by Dr. Claxton, they commonly die in convulsions,—sometimes they are dead, but still warm; and again they are cold and rigid, and the abdomen is distended with gas, showing that they have been dead for several hours.

If, then, the hæmoglobin of the red blood-corpuscles in the spleen of a septæmic rabbit may be changed into granular masses of dark pigment in the course of a few hours in mid-winter, is it very improbable that a like change may occur in the spleen, the blood, etc., of patients dead from malarial diseases, the pernicious forms of which bear a close resemblance to septæmia? I merely suggest this as a point worthy of the attention of pathologists, and not because it is necessary to defend my position with reference to the insufficiency of the evidence upon which Klebs and Tommasi-Crudeli have claimed to produce malarial fever in rabbits. (*Vide* Special Report to National Board of Health, Supplement No. 14 to Bulletin National Board of Health.)

The point I make in the report referred to is that the presence of black pigment in the spleen *of a rabbit* is not evidence that it died of malarial fever, inasmuch as rabbits dead from septæmia produced by the subcutaneous injection of human saliva may also have black pigment in their spleens. The fact that this pigment is due to post-mortem change does not weaken the argument, unless it can be shown that in the experiments of Klebs and Tommasi-Crudeli the pigment existed in the spleens before death.

Dr. Claxton cites four fatal cases in which death occurred in from twelve to nineteen days, and in which "*the spleen was normal,*" as opposed to my statement that changes in the spleen are more marked in those cases which are of longest duration. I did not refer to cases in which death occurred at so remote a period, as I believe the fatal result in these cases to be due to secondary changes, and not directly to the infectious form of septæmia resulting from the introduction into the body of the animal of the micrococcus found in human saliva. In these cases the animal

withstands the direct assaults of the parasite, but falls a victim to secondary changes resulting from its temporary presence. This view is supported by the fact that in these cases, according to my observation, the micrococcus is no longer found in the blood, and this fluid has lost its virulent character. My remarks applied to cases in which the animal succumbs to the acute infectious disease. In these the spleen has, in my experience, shown more marked changes (tumefaction, discoloration) when death occurred at the end of three or four days, than in cases terminating fatally in thirty-six or forty-eight hours, the greater number, including all of those in which my own saliva was injected.

These points, however, although worthy of the attention of pathologists, have less interest for me than has the etiological question relating to the *rôle* of the micrococcus. Dr. Claxton's results are extremely satisfactory in this regard, and I take the present opportunity for reporting some additional confirmatory experiments recently made by myself.

Experiment No. 1.—San Francisco, July 6, 1882. Injected twenty-five minims of my own saliva beneath the skin of left flank of each of two half-grown rabbits. *Result.*—Both rabbits were found dead on the morning of July 8. Post-mortem examination at 8 A.M. showed extensive cellulitis, dilatation of superficial veins, and abundant effusion of serum in subcutaneous connective tissue. This serum, and the blood obtained from the heart, swarmed with micrococci exactly resembling those heretofore found under similar circumstances in New Orleans, Philadelphia, and Baltimore.* (*Vide* Special Report to National Board of Health in Bulletin of National Board of Health, April 30, 1881.) One rabbit was still warm, the other had evidently been dead for several hours. The spleen of the first was but slightly enlarged, that of the second was swollen, hard, and dark-colored in patches. No pigment found in either spleen.

A culture-flask containing rabbit *bouillon* was inoculated with blood from the heart of rabbit No. 1. At the end of twenty-four hours the fluid in this flask swarmed with micrococci. A second culture-flask was inoculated from this, a third from the second, and so on to the sixth, twenty-four hours being allowed in each case for the development of the micrococcus.

Experiment No. 2.—July 15. Injected twenty-five minims of above culture-fluid (sixth) beneath the skin of a half-grown rabbit. *Result.*—This rabbit died during the night of July 18, and upon post-mortem examination was found to present the same pathological appearances as in the former experiment,—viz., extensive cellulitis, with effusion of serum swarming with micrococci. The blood also contained the micrococci in abundance; spleen somewhat enlarged and dark-colored; no pigment found.

A new culture was started from the blood of this rabbit by introducing a minute quantity directly from the left auricle into a culture-flask containing sterilized rabbit *bouillon*. As before, this was carried by successive inoculations from one flask to another to the sixth culture, the culture-flask being in each instance placed in an oven, at 100° Fahr., for twenty-four hours, for the development of the micrococcus.

Experiment No. 3.—July 26. Ten minims of above culture (No. 6) was injected beneath the skin of a half-grown rabbit. *Result.*—The animal died at 10 A.M., July 29, and a post-mortem examination was made at once. The subcutaneous connective tissue was, as usual, infiltrated with serum containing the micrococcus, which was also present in the blood in large numbers. The spleen was very large and dark-colored. A portion was removed for microscopical examination, and the remainder left *in situ*, the animal being so placed that it should be dependent.

No pigment was found in the portion first removed, but the presence of black pigment in the portion left *in situ* was verified the following day (removed at 9 A.M., July 30).

Remarks.—The most interesting point connected with these experiments is the fact that my saliva is as virulent now as it was in New Orleans in the summer of 1880, in Philadelphia in January, 1881, and in Baltimore in the summer of 1881. Evidently this virulence is not a temporary character due to external conditions. For nearly a year I have been residing in a very healthy climate, and have been free from septic influences such as I suggested in my first paper might account for the marked difference in virulence observed in the saliva of different individuals. This corresponds with what Pasteur has shown to be true of other septic organisms,—*e.g.*, the micrococcus of chicken cholera and the bacillus of anthrax,—viz., that varieties possessing different degrees of virulence breed true when cultivated continuously under circumstances favorable to their multiplication. In the human mouth we have a culture-chamber maintained at a constant temperature, and furnished with a constantly-renewed supply of pabulum,

* For details as to method employed, *vide* "Studies from the Biological Laboratory," Johns Hopkins University, vol. ii., No. 2, p. 164.

saliva, so that the conditions are more favorable for sustaining the physiological characters of the particular breed of micrococcus present than they could be in any artificially-conducted culture experiments.

How it happens that the micrococcus in one man's mouth possesses just the proper degree of vital activity to kill a rabbit in two days, while that from another man's mouth kills in four days, and that from another does not kill at all, is a most interesting question, and one worthy of the attention of future experimenters. I have elsewhere suggested that the supply of pabulum may be the essential point of difference, and that, under the action of the laws of natural selection, an abundant flow of saliva may favor the development in these minute plants of a capacity for rapid multiplication, a quality which would be favorable to the micrococcus when introduced beneath the skin of a rabbit, and would have a decided influence as to the date of a fatal result. The idea that the virulence of normal saliva is due to contact with ordinary septic putrefactive material—as, for example, in the post-mortem room—is opposed by the fact that putrefaction destroys this virulence, and by the results of inoculations, in rabbits, with the sputa of phthisical patients. I have now performed this experiment a number of times, and have in no case seen any evidence of septæmia resulting from it, while the local effect of such an inoculation is limited to the formation of a small abscess containing a cheesy collection of pus.

The question is frequently asked, How does it happen that man does not suffer by auto-inoculation through accidental wounds, if his salivary secretions are infected by this deadly micrococcus?

The answer is simple. The micrococcus is deadly to the rabbit, an herbivorous animal; but carnivorous and omnivorous animals—man among the number—are not so susceptible to its attacks (*vide* Special Report, *loc. cit.*, for results of experiments on dogs, rats, and fowls).

This difference may be explained in accordance with the laws of natural selection. It is evident that carnivorous animals, and our own savage ancestors, in the remote past, in their combats and struggles for food must frequently have inflicted upon each other bites in which inoculation with saliva and the micro-organisms present in this fluid would inevitably occur. Under these circumstances extermination of species, or a race-tolerance resulting from natural selection (survival of the fittest), would inevitably occur. This tolerance, in man, does not, however, seem to amount to absolute immunity, for "poisoned wounds" as the result of human bites are not unknown in surgical practice; and if these do not commonly give rise to general septæmia, they not infrequently produce local inflammation of a painful and troublesome character.

A NEW LARYNGEAL FORCEPS.

BY THOMAS AMORY DE BLOIS, M.D.

THIS instrument, which was exhibited at the Fourth Annual Congress of the American Laryngological Society, held in Boston June 12, 13, and 14, 1882, is intended to be a change from the usual form of tubular forceps, so as to obviate the necessity of changing the position of the jaws of the instrument at the moment of closure.

In Schroetter's forceps the jaws are fixed to the end of a stilet, and by the retraction of this stilet are drawn into the end of the tube, thus closing them, but at the same time causing the jaws to draw back about a quarter of an inch.

In Mackenzie's tubular forceps the stilet with the attached jaws is fixed to the handle, and the tube slides over them, closing the jaws as before, but giving a motion of translation to the point instead of one of retraction.

In my instrument the jaws of the forceps are fixed to the end of the tube, which is in its turn firmly secured in the handle. A forceps-closer, moved by a wire contained within the tube, slides over the open jaws, closing and locking them without causing any derangement of the position of the instrument at any point.

The moving parts of the forceps are covered by a metal sleeve which protects them from contact with the mouth.

The stilet and attached forceps-closer are forced forward by an arrangement of the rack-and-pinion motion worked by the ring-finger, thus gaining power and making the movement with more steadiness than when pushed directly with the thumb, as in Turck's forceps.

The handle is fitted with sockets for the

FIG. 1.

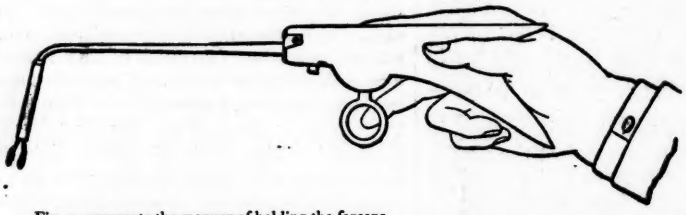

FIG. 2.

Fig. 1 represents the manner of holding the forceps.
Fig. 2 represents the jaws of the forceps closed, with the covering sleeve removed to show the moving parts.

fingers, so that the instrument may be held as one would hold a pen, and either the middle or the fourth finger is placed in the ring of the instrument. This position gives the greatest possible precision to the hand, and the least possible derangement while making traction on the ring.

In operating with this instrument, first push the ring forward to its full extent, then turn the jaws round so as to close either antero-posteriorly or laterally, according to the position of the growth in the larynx. Secondly, draw the ring a little back, so as to fix the jaws in the desired position, then grasping the instrument in the right hand, as in the cut, introduce it into the mouth with the jaws of the forceps pointing to the patient's left, turning them down after passing the tongue.

210 COLUMBUS AVENUE, BOSTON, August 12, 1882.

NOTES OF HOSPITAL PRACTICE.

UNIVERSITY OF BERLIN.

SURGICAL CLINIC OF PROF. VON LANGENBECK, BERLIN, JULY 21, 1882.

Reported by HENRY WILE, M.D.

SUPRA-PUBIC LITHOTOMY.

THE patient was a man about 45 years old, and was troubled with bladder-difficulties for many years. Thorough examination revealed calculus, and, as far as could be determined, one of unusual size.

The supra-pubic operation, or so-called *sectio altera*, was performed, and with certain antiseptic precautions without spray, but the instruments were kept in a solution of carbolic acid, the sponges were washed in a weak solution of the same acid, and the wound was several times during the operation washed out with a weak solution of salicylic acid.

The bladder was first partly distended with lukewarm water, and a sound was introduced. Then a cut about three inches in length was made in the median line of the abdomen. While cutting through the linea alba, from below upward, great care was exercised not to injure the peritoneum. Coming down upon the bladder, the sound was gently pushed forward, and a cut about one and one-half inches in length was made towards it into the bladder. The lips of the wound were held apart with tenacula, and two fingers were introduced into the bladder to ascertain the position of the stone, which was immediately removed with forceps. The stone was almost spherical, and about the size of a hickory-nut. A section was immediately made, and it was found to be composed of concentric layers around a nucleus of mucus. It was a mulberry-stone.

The wound and bladder were then thoroughly washed out through the urethra with a weak solution of salicylic acid. This was done by means of an irrigator, which consisted of a rubber tube attached at one end to a catheter and at the other to a tin vessel. The vessel was held above the patient, and the solution was allowed to flow through the catheter.

A drainage-tube was then placed into the bladder, through the wound, which latter was sewed up with interrupted sutures as far as the tube. No stitches were put into the bladder.

Prof. Von Langenbeck performed the supra-pubic operation in this case, because he thought the stone was of unusual size. He said he expected to extract a stone of the size of a pigeon's egg. Yet, as the event proved, it was not so large. However, he said that he often prefers the supra-pubic operation to operations in the perineum, on the ground that in the latter there is often considerable hemorrhage, and, what is more serious, certain nerves are cut which produce unpleasant after-effects, such as dribbling of urine, spermatorrhœa, and pruritus. He said that he had lately looked

over a number of cases in which a perineal cut was made, and in many of these cases the patients had returned with one of the above-mentioned complaints, especially dribbling of urine after urination, while in the *sectio altera* there were no such effects to be feared. He related cases where he had operated thirty years ago, and the patients are living and well to-day, never having experienced any trouble since the operation.

The only danger which he thought was to be feared in the supra-pubic operation was bad drainage in case of ulceration of the wound. But this he expects to avoid by keeping the patient in a permanent bath of lukewarm water until healthy granulation is established.

[The patient died of septicæmia about ten days after.]

CASE OF PUERPERAL CONVULSIONS TREATED WITH VERATRUM VIRIDE.—Dr. John Brown, of Williamsburg, Ohio, reports the following interesting case:

"Mrs. B., æt. 20 years; primipara. After passing a period of normal pregnancy, was taken in labor on the morning of the 17th of April. Dr. Lancaster, of Mt. Oreb, was called, and he told me that she had a moderately easy labor, and was delivered of a healthy child at one o'clock on the afternoon of the same day. After-birth expelled, together with the membranes, all in good time. Uterus contracted well, and bandage was applied. All was well until about an hour after delivery, when she complained of severe pain in the head, whereupon the doctor prescribed thirty grains of bromide of potassium, which was given. He went home, a distance of two and one-half miles, but had been there only a few minutes when they came for him in great haste, stating that they thought she was dying. He hurried to her, and found, upon his arrival, that she had just had a convulsion, and was in a state of profound sleep. As soon as she could be aroused, he administered a large dose of bromide of potassium, and continued to give it at short intervals. At the same time he gave her chloroform by inhalation unceasingly; but there was a recurrence of the convulsion in thirty-five minutes, and afterwards at intervals of thirty-five or forty minutes, until about seven o'clock, when I saw her. In about five minutes after I arrived, she was taken with the severest kind of convulsion, which lasted about three minutes, and was followed by the usual comatose state, which lasted about ten minutes, when she aroused and looked around in a frightened manner, asking what was the matter. Upon examination, we found her pulse 130 per minute, small and thread-like; temperature, 101° Fahr. We gave her at once forty drops of Norwood's tincture of veratrum viride. She passed her next time for convulsion safely, and at the end of forty-five minutes her pulse was 110, with more volume and stronger. Gave her sixty drops more, which brought her pulse down to 105 at the end of one hour and thirty-five minutes from the time she took the first dose. It continued to beat at that rate until two hours and fifteen minutes from the time of last convulsion, which was not nearly so severe as the previous one, and was not followed by the usual sleep. She remained awake, but could not comprehend fully what was said to her. She was able to take sixty drops more of the tincture, the effect of which was to bring her pulse down to seventy-two regular and natural beats per minute. She remained perfectly quiet from that time on, except that at long intervals she would seem a little nervous and excited, when we would place a handkerchief saturated with chloroform to her nose, which would quiet her again. At the end of four and a half hours from last dose we gave her twenty drops more of the tincture, with one-sixth of a grain of morphia, hypodermically, and she slept well for three or four hours, when we left her in good condition. Pulse 74; temperature 98⅘°. She made a good recovery, and is as well to-day as usual."—*Obstetric Gazette.*

CONVALLARINE.—Professor Germain Sée has brought to the notice of the Academy of Medicine a new substance, which promises to be of great therapeutic value. It is an alkaloid extracted from the *Convallaria majalis*, or the lily of the valley. This new alkaloid has been discovered by Dr. Hardy, an eminent chemist, who also discovered the alkaloid from the jaborandi, to which he gave the name of "pilocarpine." Convallarine, the name of the new substance, has been experimented with by Professor Sée at the Hôtel-Dieu in conjunction with Dr. Hardy, of which hospital the latter is the *chef du laboratoire.* Its therapeutic action is compared with that of digitalis, for which it may be with advantage substituted, as it has none of the inconveniences attributed to digitalis. Dr. Hardy was led to make researches with this plant from the fact of its being generally used by the peasants in Russia, who employ the herb in dropsies and in all cases requiring increased diuresis. According to Professor Sée, the convallarine is a powerful diuretic, and it has a marked influence on the contraction of the heart, which it regulates, while it lowers the pulse in a remarkable manner.—*Lancet.*

A NEW VARIETY OF CINCHONA.—A new variety of cinchona—cinchona cuprea—has lately been offered in the market, in which Whiffen (*Pharm. Cent. für Deutschland*) has found existing an alkaloid, which he has named "ultra-chinin," to the extent of 0.1 to 0.8 per cent. Its properties are said to be analogous to those of the other alkaloids.

PHILADELPHIA
MEDICAL TIMES.

PHILADELPHIA, SEPTEMBER 9, 1882.

EDITORIAL.

THE NORTH WOODS.

THE publication of the article "Camp Lou," first in one of the magazines and afterwards in book form, caused, last year, a rush of travel to the Adirondacks which bade fair to ruin them as a playground for the comparatively few persons who really love nature in its primeval roughness and solitude. Large numbers of sick persons, totally unfit to bear the exposure of camping out, went into the wilderness, and not a few are said to have died there. Even the author of "Camp Lou," whose "cure" had made a hospital out of the woods, himself died of consumption—so, at least, it is affirmed—last winter. As a result of these unfortunate endings, or from some other cause, during the present season the North Woods have been almost empty, in the parts we have visited not more than one-third the number of people being in that were there last year.

This is as it should be. There can be no doubt of the value of the out-door life, the pure, dry air, the freedom from all personal restraint, in the treatment of suitable cases of commencing phthisis and other diseases; but in our experience it is very necessary to select the cases carefully if good is to be achieved, and also to select almost as carefully the degree of civilization fitted for each case, because from the wigwam to the modern first-class hotel are the accommodations offered by these noble North Woods, and from the bustle of the caravansary to the solitude of a primeval wilderness is the choice of companionship. To enter into details would require more space than is at our disposal, but certain general principles may be stated as the result of a wide acquaintance with the woods and their effects upon the sick. There are three belts of territory: first, Mount Marcy and its immediate surroundings; second, the Eastern Lake District, Blue Mountain, Raquette, Big and Little Tupper, Long Lake, etc.; third, the Western Lake District, including the Fulton Chain, the Beaver River Lakes, John Brown Tract, Oswegatchie Waters, etc.

The Mount Marcy District far excels the other part in the beauty of its scenery, but can be visited only by those who are strong and well capable of much exertion. It is mostly too high for much fish or game, but it is a paradise to the pedestrian whose heart craves the pleasure of struggling up steeps twenty miles a day with a fifty-pound pack upon the back, since all the food and camp-equipage for the one or two weeks' jaunt have to be fairly shouldered.

The Eastern Lake District is the place to which eight out of every ten invalids should be sent. It affords society and comfort, with a spice of the wilderness which enables the camper-out or dweller in hotel to cheat himself into the belief that he or she is "roughing it." There black bass or pickerel may be caught in abundance, and in some places even trout are plenty, whilst the very fortunate man may get a shot at a deer, if he be patient and watch long enough.

In most portions of the Western Adirondacks game is still plenty,—"game" meaning deer and trout. When the writer first went into camp this summer, bucks and does could any sunset-time be seen playing up and down the various beaches, or feeding in the along-shore shallows of the lake. But the traveller must make up his mind to really rough it, to do without regular mails, and in going in to pass over roads compared with which riding across a granite-quarry would be travelling on a selected portion of the track on the Pennsylvania Railroad. To send to this region an invalid who de-

sires soft beds, luxurious couches, or even a moderate degree of comfort, who has no great fondness for nature, and no spirit of the sportsman, but whose chief pleasure is to be found in intercourse with his fellow-men, the newspaper, and similar earthly vanities, is like trying to cure a mangled man by fastening him on the gridiron of St. Anthony.

LEADING ARTICLES.

THE ETIOLOGY OF TUBERCULOSIS.

OUR knowledge of the etiology of tuberculosis has, by the recent discovery of Dr. Robert Koch, assumed a different aspect; and if the laborious researches of a Klebs concerning the *Bacillus typhosus*, those of Von Ziemssen and others with reference to the *bacillus* of typhus, those of Pasteur regarding the *bacillus* of anthrax, those of Wood and Formad regarding the *Micrococcus diphtheriæ*, are based upon facts, the *Bacillus tuberculosis* of Koch must be admitted as perhaps the most powerful member of that dangerous class of microzymes which, in the form of spores, rods, and dots, more than decimate the "lords of the world."

But, notwithstanding the discovery of Koch is well known, the whole *modus operandi* in the detection of these bacilli, their accurate description, as well as all the observations of the industrious investigator, have been published in but a few foreign journals, others having given extracts only. But the history of these researches, and all the facts observed by Koch, as well as the conclusions he draws from them, are so very interesting that we cannot withhold them from our readers. We present, therefore, in the following nearly verbatim translation, the lecture which was delivered on the *etiology of tuberculosis* by Koch, on March 24, 1882, before the Berlin Physiological Society, and we do this the more readily as this lecture is *quasi* a review of the whole question and of the present status of modern pathology in this direction.

It was Villemin who first endeavored to prove the possibility of transmitting, by inoculation, human tuberculosis to the lower animals. This view soon found both adherents and opponents, and for a long time a bitter fight was carried on. Until a few years ago it was a matter of doubt whether tuberculosis should be considered an infectious disease or not; but the labors of Cohnheim and Salomonsen, and, later, those of Baumgarten, who succeeded in inoculating tuberculosis into the anterior chamber of the eye, followed by general constitutional affection, and those of Tappeiner and others, who achieved the same result by the method of inhalation of the dried and powdered tubercular sputa, have at last settled this important question, and tuberculosis is now recognized by all pathologists as an infectious disease.

Statistics have proved that one-seventh of all human beings fall a victim to that merciless destroyer of the human race, tuberculosis, and that of the productive classes in middle life fully one-third die of this scourge of humanity. That public hygiene must, therefore, pay the utmost attention to a possible prevention of tuberculosis, and especially to its relation to the *Perlsucht* of our domestic animals, will fully be made clear in the following. It was mainly the latter point which induced Koch to inquire deeply into the etiology of tuberculosis.

All experiments tried so far with the view of detecting the real cause of this disease had been unsuccessful, because all the usual processes of coloring pathogenic microorganisms failed in tuberculosis; so that all efforts to isolate and cultivate the virus of tubercle were necessarily frustrated, and Cohnheim was forced to admit, in the latest edition of his work on general pathology (January, 1882), "*that the direct proof of the tubercular virus and its tangible demonstration were a problem unsolved to-day.*"

Koch in his investigations also at first made use of the former methods, and met with the same want of success, till he at last, almost by accident, was induced to leave the beaten path, and to try another, which happily led him to positive results.

He first directed his examination to the detection of any foreign parasitic bodies which might possibly serve as pathogenics, and he really succeeded in finding, by a peculiar process of coloring of his own, in all tissues which were the seat of morbid alteration by tubercles, *characteristic bacteria until then unknown.*

The method of procedure employed by him is as follows:

The objects to be examined are first prepared in the usual way for the detection of pathogenic bacteria, and either spread, dried, and heated on the cover-glass, or cut into slices after hardening in alcohol. The cover-glasses, or the slices, are then placed in a coloring solution of the following composition. Two hundred cubic centimetres of distilled water are mixed with one cubic centimetre of a concentrated alcoholic solution of methyl-blue, and well shaken, and then two-tenths cubic centimetre of a ten-per-cent. solution of caustic potash are added under continuous shaking. This mixture must not cause any precipitate or sediment, even after having been kept for several days. The objects to be colored are left in this solution from twenty to twenty-four hours. If the coloring solution is heated in the water-bath up to 40° C., the length of time may be shortened to from one-half to one hour. A concentrated aqueous solution of *vesuvin*, which has to be filtered each time immediately before using it, is then poured over the cover-glass, which latter, one or two minutes later, is rinsed in distilled water. When the cover-glass is taken out of the coloring solution, the pathological object upon it has first a dark-blue color, the coloring being in surplus; but after treatment with the vesuvin solution this blue color disappears, and the specimen assumes a light-brown tint. If now placed under the microscope, all parts of animal tissues, especially the contents of cells, nuclei, and their products of decomposition, have a brown color, but the bacteria of tuberculosis appear in a beautiful blue tint. Koch found that, with the exception of the bacilli of lepra, under this process even all other bacteria take on a brown color. The contrast in color between the brown of the tissues and the blue of the tubercle-bacteria is so great that the latter are immediately recognized, even if present in very small numbers only.

In a very similar way the slices have to be treated. From the solution of methyl-blue they are placed into the filtered solution of vesuvin, kept in this from fifteen to twenty minutes, and then rinsed in distilled water till the blue color has disappeared and the slices have assumed a brown tint. They are then freed of their water by absolute alcohol, cleared up in oil of cloves, and either examined under the microscope in this oil, or placed in Canada balsam. In these preparations the tubercle-bacteria also appear of a blue tint, while the tissues have a brown color.

These bacteria are, however, not only colored by methyl-blue; with the exception of brown coloring matters, they are acted upon also by other aniline colors, if made with an alkaline solution; but the bacteria appear best with methyl-blue. In the procedure described, instead of the potash solution, sodium or ammonium may be substituted, from which the deduction can be made that no importance is to be attached to the potash, but that a strong alkaline solution is absolutely necessary. It has been found that, if the percentage of the potash solution is still increased, the bacteria appear where the weaker solution did not bring them to light; but a stronger alkaline solution has such a damaging influence on the tissues themselves that it can be employed with advantage only under special circumstances, and after an earlier examination has been made with the ten-per-cent. solution.

Koch says that the bacteria so treated are very peculiar in appearance. "They have a rod-like shape, and belong, therefore, to the group of bacilli. They are very thin, and from one-fourth to one-half as long as the diameter of a red corpuscle; but sometimes they may grow to a length of fully the diameter of a red blood-corpuscle. As regards their shape and size, they are remarkably like the bacilli of lepra, but differ from them in being somewhat more slender and pointed at the ends. Besides, the lepra-bacilli are colored by the nucleus-coloring process of Weigert, while the tubercle-bacilli are uninfluenced by the same. At all points where the tubercular process is either beginning or in rapid progress, the bacilli are found in large quantities; they form then small, compact groups, sometimes arranged in bundles, frequently being met with in the interior of cells, and often presenting the same picture as the lepra-bacilli, collected in cells. But, besides, numerous free bacilli are also seen; especially on the edges of larger caseous *foci* the bacilli are observed in masses, and not included in cells.

"As soon as the acme of tubercular eruption is past, the bacilli are rarer, are met with only in very small groups or single at the edge of the deposit, while a

little farther away the blue color becomes lighter and lighter, showing evidently bacilli already dead or dying. They may disappear altogether, but this is rare; and if they are absent, it is only on places where the tubercular process has come to a stand-still.

"If giant cells are present in the tubercular tissue, then the bacilli are usually collected within them. In cases of very slowly progressing tuberculosis, these giant cells are commonly the only places in the interior of which the bacilli can alone be found. In such cases the majority of giant cells encircle one or two bacilli. The picture presented under these circumstances is in reality a surprising one: in long-continued passages of a slice, fresh groups of giant cells appear rapidly before the astonished eye; almost every individual cell encircles in its wide space filled with brown-colored nuclei one or two very diminutive blue rods, which float nearly in the very centre of the giant cell. Often the bacilli are met with in small groups of giant cells, sometimes only in single cells, while numerous other giant cells do not contain any. Then, as can be judged from their size and position, those cells which are inhabited by bacilli are young, of recent formation, while those free of these bacteria are older; and it may be supposed that once these also contained bacilli, but that the latter either died or passed over into their permanent condition, of which later more will be said. Analogous to the formation of giant cells around foreign bodies, as vegetable fibres and Strongylus eggs, as described by Weiss, Friedlaender, and Lanlamié, we have to suppose the relation of these cells to be to the bacilli. Undoubtedly the giant cells were formed to encircle the bacilli as foreign bodies; and if in a tubercular tissue such cells are found empty, the supposition is justified that they once contained the bacilli which gave origin to them.

"The bacilli may also be recognized unprepared by coloring. For this purpose it is necessary to examine specimens of such parts as contain large quantities of bacilli,—*i.e.*, a gray tubercular nodule from the lung of a guinea-pig having died from inoculated tuberculosis. The object is placed with blood-serum into the hollow of an excavated slide. The bacilli appear then as extremely small rods, showing molecular motion, *but not the least self-motion.*

"Under certain circumstances, later to be explained, the bacilli form spores in the animal body. Single bacilli contain then mostly two to four spores, of oval shape, and spread in equal distances over the length of the bacillus."

As regards the presence of bacilli in the different tubercular affections of men and animals, Koch has had thus far the opportunity to examine the following material:

I. Of the Human Being.—*Eleven cases of miliary tuberculosis.*—Koch never missed the bacilli in the miliary tubercles of the lungs. Often, in such nodules, the centre of which did not receive any coloring of the nuclei any more, no bacilli could be found, but then they were met with at the margin of the tubercle in small groups, and in younger nodules, the centre of which was not as yet cheesy-degenerated, the bacilli were noted in much larger quantities. They could, besides, be demonstrated in the miliary tubercles of the spleen, liver, and kidneys. They were very numerous in the gray nodules of the pia mater in basilar meningitis. In several of the cases examined, bronchial glands, which were in a state of cheesy degeneration, contained partly large masses of bacilli, and among them many with spores, and partly tubercles embedded in the glandular tissue, with a giant cell in the centre, surrounded by epithelioid cells, and a few bacilli in the interior of the giant cell.

Twelve cases of caseous bronchitis and pneumonia (in six cases formation of cavities).—Here the bacilli were mostly found at the margin of the cheesy-infiltrated tissue only, but there they were very numerous. Also in the interior of the infiltrated portions of the lungs, nests of bacilli were sometimes noted. Usually, in most cavities, the bacilli are exceedingly numerous. The small cheesy crumbs in the cavities consist mainly of bacilli masses. Occasionally many bacilli with spores were met with in the soft, cheesy pieces ot cavities. In large vomicæ these bacilli were accompanied by other bacteria; but as, by the coloring process described, only the tubercle-bacilli assume a blue tint, they were easily distinguished from the others.

One case of a single tubercle (larger than a hazel-nut) *of the brain.*—The cheesy mass of the tubercle was surrounded by a tissue rich in cells. In this tissue many giant cells were embedded. Most of the latter did not contain any parasites, but here and

there groups of giant cells were met with, each of which contained one or two of the bacilli.

Two cases of intestinal tuberculosis.—In the tubercular nodules grouped around the intestinal glands, the bacilli could be demonstrated very plainly, and here also they were found especially numerous in the younger and smaller nodules. They were seen also in the mesenteric glands.

Three cases of scrofulous glands recently extirpated.—Only in two of them bacilli enclosed in giant cells were noted.

Four cases of fungoid inflammation of the joint.—Here also in two cases only, and in small separate groups of giant cells, bacilli were detected.

II. Of Animals.—*Ten cases of Perlsucht*, with calcareous nodules in the lungs, in some cases also in the peritoneum, and in one in the pericardium. In all these cases bacilli were met with, and mainly in the interior of giant cells, which were present in the tissues surrounding the calcareous masses. The bacilli are generally so evenly distributed that among the numerous giant cells rarely one was seen which did not contain one or more, and sometimes as many as twenty, bacilli. In one case the bacilli were observed also in the bronchial glands, and in one other in the mesenteric glands.

Three cases in which the *lungs of cattle* did not present the well-known calcareous nodules with uneven surface, but smooth round nodules filled with a soft, cheesy mass. This form is usually not considered as *Perlsucht*, but as bronchiectasis. In the neighborhood of these smooth nodules, giant cells with tubercle-bacilli were noted.

A lymphatic calcareous gland of the neck in a pig contained also bacilli.

In the organs of a chicken which had died of tuberculosis, large quantities of bacilli were met with,—viz., in the tubercular nodules in the cord, and in the peculiarly large nodules of the alimentary canal, of the liver, and of the lungs.

Of three monkeys that died of tuberculosis, the lungs, spleen, liver, omentum, all thoroughly infiltrated with numerous nodules, and the cheesy lymphatic glands, were examined, and bacilli found in the nodules or their immediate neighborhood.

Of other animals suffering from spontaneous tuberculosis, nine guinea-pigs and seven rabbits were examined. *They all contained bacilli in the tubercular nodules.*

Koch investigated, besides, a large number of animals which had become the victims of tuberculosis by *inoculation.* The latter had been performed with all kinds of tubercular material,—viz., with gray and cheesy tubercles of human lungs, sputa of phthisical persons, tubercular masses of monkeys, rabbits, and guinea-pigs spontaneously diseased with tuberculosis, etc. The number of animals infected in this manner was one hundred and seventy-two guinea-pigs, eighty-two rabbits, and five cats. Their investigation had to be confined to the tubercular nodules of the lungs. *In all these the bacilli were not a single time wanting.*

That the bacilli had never been found before, Koch explains by the fact that the bacilli are so exceedingly small and generally only few in number, especially when their presence is confined to the interior of giant cells, when they necessarily will escape the most patient observer, unless they have been colored by the process described. Koch further mentions that Schüller had already noticed micrococci in tubercular nodules, and that Klebs and Aufrecht (in his pathological communications) say that they had seen, besides micrococci, very small and short rod-like formations. These investigators never imagined, however, that these were the pathogenic bacilli of tuberculosis, as, in consequence of their not being able to show them by the coloring process, they met with them rarely only.

"*Based upon my very numerous observations*," says Koch, "*I consider it proved that in all tubercular affections of men and animals these tubercle-bacilli are present, which have been described by me, and which are distinguished from all other micro-organisms by the peculiarities mentioned. But this coincidence of bacilli and tubercular affections does not permit the conclusion as yet that these two appearances* (*bacilli and tubercles*) *are necessarily in causal connection*, though the probability for this assumption becomes great from the fact that these bacilli are found especially where the tubercular process is in its beginning or in progress, while they disappear where the disease has come to a stand-still."

To prove, however, that tuberculosis is a parasitic disease, which is caused by the immigration of bacilli, and which is progressing *a priori* by the growth and propagation of these micro-organisms, Koch undertook to isolate the bacilli from the

body, to propagate them by *pure-culture* until they were freed from any possible morbid product derived from the animal organism, and at last, by transferring the isolated bacilli to healthy animals, to bring about the same morbid process of tuberculosis, of which experience has demonstrated that it is produced by inoculation of tubercular material of natural origin.

The principle of the method made use of for this purpose by Koch was based upon the employment of a *solid*, transparent culturing soil, which even at breeding temperature would retain its solid consistence. The known advantages of the method of pure-culture, introduced by Koch for the investigation of bacteria, enabled him to solve the difficult problem of the pure-culture of the tubercle-bacilli.

Serum of cattle-blood or of sheep-blood, as pure as possible, is poured into a perfectly aseptic reaction-glass, closed by a stopper of cotton wadding, and for one hour daily during six days heated up to a temperature of 58° C. By this method, if not always it is at least mostly possible to make the serum perfectly sterile. It is then heated to 65° C. for several hours, and until it just becomes stiffened and solid. After this treatment, the serum appears as an amber-yellow, perfectly transparent or only slightly opaque, solid, gelatin-like mass, which, even if for several days continuously exposed to the breeding temperature, must not show the least development of bacteria. If the temperature is above 75°, or the serum exposed to it too long, the latter becomes totally transparent. To get for the culture a surface as large as possible, the serum is allowed to stiffen while the reaction-glass is held in the most slanting position. If the culture has to be ready for immediate microscopical examination, the serum is stiffened in a watch-glass.

Upon this stiffened blood-serum, forming a transparent soil, which at breeding temperature continues solid even, the tubercular material is placed in the following manner. We mention first as a condition *sine qua non*, as of paramount importance, that every instrument whatever used in this procedure must at first have been made thoroughly aseptic by exposing it to white heat. The experiment will succeed almost in every case, if an animal is at disposal which has just died of tuberculosis or has been killed for this purpose. The skin over the chest and abdomen is first dissected off, the ribs are then separated, the anterior wall of the thorax removed without opening the abdominal cavity, and the lungs laid bare. The instruments are now again changed for others, disinfected in the same manner; single tubercular nodules, or parts of them, of the size of a pin's head are quickly cut out, and carried with the aid of a previously thoroughly heated platinum wire, inserted into a glass rod as handle, upon the culturing soil in the reaction-glass. The stopper of cotton wadding must be removed only for as short a time as absolutely necessary. In this manner about six to ten glasses are provided with tubercular material, such a number being necessary, as with the utmost caution some accidental impurities cannot always be avoided. Lymphatic glands, the cheesy degeneration of which has just begun, can be made use of as well as tubercular lung-nodules; pus of softened glands, however, will not answer, rarely containing bacilli.

More difficult is the culture of bacilli from human tubercular organs, or from a lung the seat of *Perlsucht*, as these often contain many septic bacteria. Frequent rinsing with solutions of corrosive sublimate may prevent their admixture.

The reaction-glasses, provided in the manner described with tubercular material, are then placed into the perfectly aseptic breeding apparatus, and kept constantly exposed to a temperature of 37° to 38° C. During the first week no change can be noted. But should a change take place within the first few weeks and bacteria develop themselves either on the tubercular material or even at a distance from it,—generally to be recognized by white, gray, or yellowish drops, often also by the serum becoming liquid,—then impurities have been present and the experiment has been unsuccessful.

The cultures caused by the growth of the tubercular bacilli appear to the naked eye in the second week, generally not before the tenth day, as very small dots and dry scales, which encircle the tubercular particle in a larger or smaller circle according as the tubercular material has been spread more or less over the whole culturing soil. If only a few bacilli have been present in the original seed, it is hardly possible to separate them from the tissues and to plant them immediately

upon the culturing soil; while this can easily be done if the bacilli have been numerous. One notes, for instance, in particles of scrofulous glands, dark and white dots, their color depending upon the direction of the light. With the aid of a magnifying-glass (thirty to forty times) the bacilli-colonies can be recognized by the end of the first week. They appear as *very neat, spindle-shaped, and mostly S-formed structures;* also in other similar shapes, which, when spread on the slide, colored, and placed under a powerful microscope, consist only of extremely fine bacilli. To a certain degree the growth of these colonies progresses in the course of three to four weeks; they enlarge and become flat, scale-like pieces of nearly the size of a poppy-seed; they lie loose on the culturing soil, and never penetrate of themselves into the latter or liquefy the same. The colony of bacilli forms, besides, such a compact mass that the small scale can easily be lifted from the stiffened serum as a whole and unbroken. In reality a certain pressure is necessary to break them. The remarkably slow growth, possible only at breeding temperature, then the peculiarly scale-like, dry, and solid consistence of these bacilli-colonies, is not met with in any other known kind of bacteria, so that mistaking tubercle-bacilli for others, or not recognizing any impurity, is almost an impossibility after a very little practice. The growth of the bacilli ends after a few weeks, and a further enlargement of them probably does not set in, because *the tubercle-bacillus possesses no self-motion whatever*, and the process of growth alone changes slightly their position on the culturing soil, and this takes place only in very small dimensions, on account of the very slow propagation of the bacilli. To keep such a culture going, it is necessary to place it, after about ten to fourteen days, upon a new culturing soil. This is done by taking up a few scales with the disinfected platinum wire and carrying them to a fresh, sterile, and stiffened blood-serum contained in a reaction-glass, where they are spread as much as possible over the culturing soil. Here again, in the same length of time, scale-like dry masses form. In this way the cultures are carried on. Other culture-soils might be prepared, but this is the easiest and most practicable.

In the beginning Koch took only the tubercle-bacilli from the lung-tubercles of guinea-pigs infected by tubercular masses. He found them most developed in the lungs, and less in the abdominal organs. Koch also observed that, if several healthy guinea-pigs were kept in the same box with those infected by tubercular inoculation, the first soon became affected also, and the swelling of the bronchial glands and the beginning of the process in the respiratory organs proved to him that *the spontaneous tuberculosis* of these animals was due to *inhalation* of tubercular matter, developing itself from one or two bacilli perhaps only, and progressing, therefore, in general so very *slowly*.

The fact is well known that if of married persons, sleeping together in one bed, one dies of tuberculosis, the same disease, attacking the surviving husband or wife, generally develops a comparatively long time afterwards, and very gradually, and progresses very slowly. The observation made by Koch would tend to explain this slowness and want of activity.

Different is the result of inoculated tuberculosis. The inoculation was generally performed in animals on the abdomen near the inguinal glands. The latter first commenced to swell, and gave, therefore, an early and very reliable indication of the success of the inoculation. Here the disease—as from the beginning a greater quantity of the infectious material was introduced into the system than can be done by inhalation—runs a far more rapid course than spontaneous tuberculosis, and on dissecting such animals, the spleen and liver were always found to be far more attacked by the tubercular process than the lungs.

According to Koch, it is, therefore, not difficult to recognize, in animals selected for experiments, those affected with spontaneous and those suffering from inoculated tuberculosis.

Employing every possible caution (previous disinfection of the integument, use of disinfected instruments, etc.), at one and the same time four to six guinea-pigs were inoculated in the manner described with the tubercular material, the virulence of which was to be determined. *The success was always the same uniform one;* in all animals which had been inoculated with fresh particles containing or rather consisting only of tubercle-bacilli, resulting from pure-culture, the small wound made by the inoculation was generally glued to-

gether by the following day; it remained the first eight days unchanged; then a small nodule formed, which either enlarged without bursting, or, as usually happened, was transformed into a dry, flat ulcer. Two weeks after inoculation the inguinal glands on the side of the wound, and sometimes also the axillary glands of the same side, were swollen to the size of a pea. From that time the animals rapidly emaciated, and either died within from four to six weeks or were killed to prevent any possible complication by spontaneous tuberculosis.

That in these cases the tubercular infection was caused by the inoculation alone of the tubercle-bacilli can, according to Koch, be proved from the fact that, *while without exception each of these animals was within four weeks tuberculous in a high degree*, in a large number of experiments where the inoculation was performed with particles containing *no* tubercle-bacilli, as pieces of a scrofulous (not cheesy) gland, fungoid masses of a joint, lung-tubercles of a monkey which had been dried in extreme heat for the time of two months, and such as had been kept one month in alcohol,—in all of which the absence of the bacilli had previously been verified,—*not a single* animal showed any signs, after four weeks had passed by, of having become affected with tuberculosis.

Of such guinea-pigs as had been infected by inoculation with tubercles of the monkey's lung, with miliary tubercles of the brain and lungs of men, with cheesy masses of a phthisical lung, with tubercular nodules of the lung and the peritoneum of cattle affected with *Perlsucht*, *cultures of tubercle-bacilli* were then instituted. It was found that, just as the picture of the disease caused by the different enumerated substances in the guinea-pig is invariably the same, the cultures of bacilli derived from the different cases did not differ in the least from one another.

Altogether fifteen such pure-cultures of tubercle-bacilli were made,—four of guinea-pigs inoculated with monkey-tuberculosis, four with *Perlsucht*, and seven of guinea-pigs inoculated with human tubercular matter.

But to exclude the objection that by the preceding inoculations of the tubercular masses in guinea-pigs a possible alteration in the nature of the bacilli might have been produced, making the formerly different organisms *quasi* alike, Koch endeavored to culture the tubercle-bacilli immediately from such by tuberculous spontaneously diseased organs of human beings on animals. These experiments were a number of times successful, and pure-cultures were obtained from two human lungs with miliary tubercles, from one such lung attacked by caseous pneumonia, twice from the contents of small cavities of phthisical lungs, once from cheesy mesenteric glands, and twice from scrofulous glands recently extirpated; further, twice from the lung of a cow suffering from *Perlsucht*, and three times from the lungs of guinea-pigs attacked with spontaneous tuberculosis. *These cultures also were exactly alike*, and also those which were carried first through guinea-pigs inoculated by them, so *that the perfect identity of all bacilli met with in all different tubercular processes cannot be doubted.*

In reference to these pure-cultures Koch mentions also that he could state, contrary to Klebs, Schüller, and Toussaint, who in their culture of micro-organisms from tubercular masses found that the culture-fluids, after their infection with tubercular material, became opaque from two to three days later and contained many bacteria, that the tubercle-bacilli in a fluid grew very sparingly only, that such a fluid does not become opaque, as the tubercle-bacilli possessed no self-motion, and that if a growth did take place, it did so only after three to four weeks, so that the conclusion is evident that the investigators named had made their experiments *with other organisms*, but not with tubercle-bacilli.

Koch's observations have demonstrated, therefore, *that the presence of characteristic bacilli is regularly connected with tuberculosis, and that the bacilli can be taken from tubercular organs and be isolated in pure-cultures.* The important question had still to be answered, if the isolated bacilli, when again introduced into the animal body, were capable of reproducing the same morbid process of tuberculosis. To exclude in the solving of this question—the chief purpose of all investigations of the tubercular virus—any possible errors, many different kinds of experiments were instituted, the details of which may be imagined from the preceding.

Koch instituted first a series of experiments with simple inoculation of the bacilli in the manner described, by which it

was found that, if the inoculation was made in the neighborhood of the inguinal glands, the morbid process following was exactly the same as the one mentioned above as taking place after the animals were inoculated with fresh tubercular masses.

In other experiments the bacilli were inoculated into the anterior chamber of the eye of guinea-pigs, to note if the same effect would result with the artificially developed tubercular virus as when the natural virus was used. It was found that, if the smallest possible number of bacilli were employed, the result was the same as the one reported by Cohnheim, Salomonsen, and Baumgarten, who experimented with natural tubercular masses. Notwithstanding these convincing proofs, Koch instituted still other experiments, injecting the bacilli-cultures into the abdominal cavity or directly into the circulation, and, lastly, he tried these experiments also on those animals (rats, rabbits, and dogs) in whom infection with tuberculosis is not easily successful. He found that there was no difference in the condition of the lung or the other organs of the animals infected with the different cultures; *in all animals* numerous miliary tubercles were noted in the lungs; also the liver and the spleen of all these animals contained extraordinarily many tubercles; but in those that died first, these tubercles were microscopically small; in those that died later, they were visible to the naked eye; and in one rabbit there were met with also in the omentum, the diaphragm, and the mesentery miliary tubercles recognizable with the naked eye. *Two control-animals* were dissected, and in no organ was there seen any tubercular deposit.

Frequently the tubercular nodules, which had been caused by vaccination as well as by injection of the bacilli-cultures, were examined with the microscope and found perfectly identical with the tubercles which are usually met with in animals affected with the common spontaneous tuberculosis, or with tuberculosis developed after inoculation with tubercular material. Their structure and everything was alike. From these nodules again bacilli-cultures were instituted, and these again employed for inoculation. The result was always the same: the same general tuberculosis followed.

"Reviewing all these experiments," says Koch, "I find that of the large number of animals to whom the bacilli-cultures were transmitted in very different ways,—by simple injection into the areolar tissue, by injection into the abdominal cavity, or into the anterior chamber of the eye, or by direct injection into the circulation,—all without exception became tuberculous, and not only single nodules developed themselves, but the extraordinarily large number of tubercles corresponded to the great number of the germs of infection introduced in this manner into the system. In other animals, by inoculating the smallest possible number of bacilli into the anterior chamber of the eye, I succeeded in producing the same tubercular iritis which was the result of the inoculation of genuine, natural tubercular material, as performed by Cohnheim, Salomonsen, and Baumgarten."

Koch demonstrates clearly by control-animals, and by the whole aseptic method of procedure, that a mistake with spontaneous tuberculosis or an accidental, unintentional infection of the animals experimented upon with tubercular virus is totally excluded, and that he is justified therefore in contending—

That the bacilli met with in the tubercular material are not accompanying the tubercular process, but the cause of the same, and that we possess in the tubercle-bacilli the actual tubercular virus.

"And so," concludes Koch, "we have gained at last the necessary knowledge to define exactly the disease which we understand by 'tuberculosis,' a thing impossible before. A definite criterion for tuberculosis was wanting: one considered miliary tuberculosis, phthisis, scrofulosis, *Perlsucht*, etc., all one and the same morbid process, while another, with equal right, took them to be different maladies. In future, it will not be difficult to say what is tuberculosis and what not. Not the peculiar structure of the tubercle, not its want of blood-vessels, not the presence of giant cells, will determine the question, but the demonstration of tubercle-bacilli either in the tissue by color-reaction or by culture upon stiffened blood-serum. Considering this criterion as a guide, we have, according to my investigations, to believe miliary tuberculosis, caseous pneumonia, cheesy bronchitis, tuberculosis of the intestines and of glands, *Perlsucht* of cattle, spontaneous and inoculated tuberculosis of animals, all to be identical. As regards

scrofulous and fungoid affections of joints, my investigations have not as yet been numerous enough to enable me to form a judgment. Undoubtedly a large part of scrofulous affections of glands and joints belong to genuine tuberculosis. The fact of my having found tubercle-bacilli in the caseous glands of a pig, and in the tubercular nodules of a hen, seems to justify the idea that tuberculosis is spread more among our domestic animals than is generally supposed, and it would be very desirable to investigate this subject still further."

Koch endeavors also to answer the question, Whence come these parasites, and how do they get into the body? He reminds us that the tubercle-bacilli grow only at a temperature of 30° to 40° C., while below 30° and above 42° within three weeks no growth was noted, while, for instance, the bacilli of anthrax grow decidedly even at 20°, and between 42° and 43° C., and he comes to the conclusion that, as in moderate climates outside the animal body no temperature above 30° C. ever continues evenly for two weeks, the bacilli are confined for their process of development and growth to the animal organism, and that they are therefore not accidental but genuine parasites, and are derived from the animal organism.

As regards the second question, Koch draws our attention to the fact that the vast majority of cases of tuberculosis have their beginning in the respiratory passages, and that the infectious material becomes first apparent in the lungs or in the bronchial glands, so that the idea lies near, *that the tubercle-bacilli are usually inhaled with the atmosphere, being attached to dust-particles.* The manner in which they get into the air is made plausible if we remember in what enormous quantities the tubercle-bacilli, which are sojourning in the cavities, are expectorated by phthisical persons with their sputa, which are wafted in all directions.

To get an idea of the presence of tubercle-bacilli in such sputa, Koch has frequently examined those of a large series of consumptives, and found that, while some sputa contain none, in about half the cases these sputa are the seat of an enormous number of bacilli, among which were many with spores. It must further be mentioned that Koch never was able to detect these bacilli in the sputa of non-phthisical persons, notwithstanding he examined about an equal number of such. Animals inoculated with such fresh sputa, containing bacilli, became just as surely tuberculous as if inoculated with miliary tubercles. But even the process of drying did not deprive such sputa of their virulence.

Four guinea-pigs became just as tuberculous by inoculation of sputum dry and two weeks old, four others by such four weeks old, and four others by such eight weeks old, as after infection with fresh material.

Koch draws the conclusion from this that dry phthisical sputa sticking to the floor, clothing, etc., keep their virulence for a long time, and if inhaled as dust into the lung may cause tuberculosis. He thinks that the duration of virulence depends upon the formation of spores, which goes on in the animal organism, and not outside of it, as is the case with the bacillus of anthrax. *The period of latency seems to be from ten days to three weeks.*

Concerning *acquired* and *inherited* disposition, Koch does not wish to give his opinion as yet, as his investigations in this respect have not been concluded as yet. He only says that we should remember the *very slow growth of the tubercle-bacilli*, and that if they are not directly introduced into the system they will not develop further and will not cause tuberculosis. If placed on a superficial wound in the skin, or upon the cornea, they will very exceptionally only induce general affection. Possibly there must be in the usual way of infection certain conditions favoring the infection, "the nestling of the bacilli," as stagnant secretions, a peculiar morbid alteration and *dénouement* of the mucous membrane of its protecting epithelium, etc. Otherwise it could hardly be explained, why every human being does not fall a victim to that disease, especially in densely-populated districts.

We only hope that these laborious researches of Koch will soon cause favorable therapeutical results, and first of all preventive measures. We must see that the great source of infection—the sputa of phthisical persons—is done away with by their immediate destruction, and by preventing their being drifted away with the air. We must further prevent the eating of meat of domestic animals affected with any form of tuberculosis, and pay especial attention that the milk of such cows is not brought into commerce.

One thing is certain: public hygiene has now made such immense progress that no civilized government can well exist without having medical men as advisers in professional matters. The United States of North America is the only civilized nation where the machinery of government is not provided by law with a board of medical counsellors. The Department of the Secretary of the Interior of the national government, and of every one of our States, should have two great subdivisions,—one for educational and one for medical affairs.

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LONDON LETTER.

THE great event of the medical profession at the present time has been the Jubilee Meeting of the British Medical Association in the city of its birth, Worcester, on the Severn. When Ceawlin and his Wessex men first pushed up the valley of the Severn they noticed how fertile a plain it was. The old Cymri knew that as well as the invaders, and fought hard to keep it. In later times Worcester was one of the loyal towns of the Welsh Marches, and has the name of "the Faithful City," for its fidelity to the royal cause. The Scots of the Stuart dynasty always aimed at reaching Worcester, and here one of the decisive battles of Oliver Cromwell was fought. After his victory the prim old Puritan stabled his horses in the beautiful chancel of the cathedral, in which lie the remains of King John, the worst of the Angevin kings of England. In Worcester, fifty years ago, dwelt Charles Hastings, the son of the worthy centenarian vicar of Martly. He lived a life of usefulness, crowned by his founding the British Medical Association. At first it was the *Provincial Medical and Surgical Association*, to give to provincial medical men the opportunity of meeting and interchanging views and opinions, as was done in the metropolis. Fifty of the leading men of the Midlands and the West gathered together at the call of Hastings, who read a paper on the object of the Association. The first President was Dr. Johnson, of Birmingham. With Hastings were associated Dr. Kidd, Professor of Physic at Oxford, Dr. Corrie, of Birmingham, Dr. Conolly, of Cheltenham, Mr. Soden, of Bath, Dr. Evans, of Ross, Mr. Hellings, of Bristol, and others. The Association held its meetings year by year in various provincial towns, and it was not till 1862 that it visited the metropolis. Dr. Hastings was ultimately knighted for his various services to the public. He lived to watch over his promising bantling till it numbered two thousand five hundred members when it met at Chester in 1866. Since then it has grown to four times that size. At first its proceedings were recorded in a volume of Transactions, but this in time gave place to the present "*British Medical Journal; being the journal of the British Medical Association.*" Some years ago it became an incorporated society for business purposes. Its growth justifies the wisdom of the original founders, and shows that they knew what they were doing. Its great utility in the calling of men together from all parts of the kingdom, so that personal acquaintance welds the body into a solid whole, is admitted by all. At first it struggled on in dire poverty, in debt, indeed, and somewhat despised. In part it had outgrown the original aim. Hastings was gone, and the other men did not quite know how to steer the bark.

The admission of the metropolis altered its primitive character; its editor now lived in London, its journal was published in London, while its metropolitan element was throwing the original provincial element into the background. But this Jubilee Meeting promises to restore to the Association its provincial character. Last year the meeting of the International Medical Congress dwarfed the Association's meeting to a small gathering at Ryde, in the Isle of Wight, under the presidency of Benjamin Barrow, a man proportioned to the dimensions of the meeting. This year Mr. Barrow once more emerged from his wonted obscurity to show himself in public and introduce his successor, Dr. Strange, of Worcester, a man of larger growth, to preside over a more important gathering. Dr. Strange commenced his address by bidding all welcome to "the Faithful City," of which it is said, "the girls of Worcester are poor, proud, and pretty." He gave a sketch of the masters of medicine in the old time, and then onward. His sketch of the provincial medical man at the time of the founding of the Association was, in his own words, as follows: "With the exception of a few local physicians of the older stamp, solemn, scholarly, and formal, and here and there an apothecary of more than ordinary acuteness of observation, there existed one dead level of mediocrity,—men without the ambition to compete with their metropolitan brethren, because the means of doing so were denied them. No sparks of genius emanated from their brains, because there was no mental friction to produce them. No doubt it was the superior education of the general practitioner that made literature distasteful to him, and scientific attainments rare, whilst the desire for improvement, which might casually arise, found no field for action. So he settled down into the mere copier of other men's prescriptions, and the collector of current nostrums for certain symptoms. Bundles of prescriptions were handed down from one

practitioner to another along with the practice. Having no other idea than that disease was an entity, he set to work to drive it out of the system by the popular means of bleeding, purging, and sweating." He then paid an appropriate tribute to the *Lancet* for what it had done for the profession. Dr. Strange, it seems, is as little satisfied with the metropolitan consultant of to-day as with the rural practitioner of fifty years ago. This is what he thinks of the class to which the writer belongs: "And then as regards consultants. Do we not recognize a solemn farce when Mr. A. or Mr. B. returns from consulting, say some metropolitan celebrity, and tells us that Dr. C. has laid down all the rules for his future life, and indicated this or that health resort as essential to recovery, and all in ten minutes' time, and for a fee of a guinea? The issues of life and death in the case of a stranger, never seen before, solved in a ten or fifteen minutes' interview, and all for one guinea! Why, a lawyer would take six weeks to do the same amount of work, and charge a bill of fifty pounds." He hit a weak spot there. Grave issues ought to have full deliberation given them, that is only fair to the patient, and the doctor should be paid accordingly, that is but just to the doctor, only most of us do not dismiss a case in fifteen minutes, and certainly we do not take one guinea, except where we have reason to believe the patient's means are limited; and we further assert the right of private judgment, to take no fee at all if we think proper. Then he went on to say, "The public likes to be bequacked, and bequacked it will be:" so the public are no more enlightened than the profession! He then urged "a more intimate connection between the branches of the Association and the governing body, so that the committee of council would become in fact, as it now is in theory, really and perfectly representative,"—a little slap at the committee of council quite called for by the existing state of affairs. Then followed the annual report, read by the Secretary, which told of the material prosperity of the Association, the increase in its members; indeed, all was rosy without, however things might be within. The first meeting concluded with a discussion on the position of homœopathists and their relation to the Association. There was to have been a lively scene on the term of office of the editor. I had given notice a year before that I should move an alteration of a by-law, so that the editor be elected for five years, leaving him eligible for re-election if approved. Of course the friends of the editor were prepared to oppose this: so they fixed the first night for the discussion of the question. This seemed to me unwise, and that it would be better to let the members have time to talk the matter over among themselves before they formally voted on the matter. So I wrote accordingly. But the powers ruled that a time had been given me, and if it was not kept, so much the worse for me and my motion. Knowing I would not be present, my name was called. Next morning I presented myself before the President in general meeting to explain my non-appearance, but before I could finish my brief explanation the president of council ruled me out of order, and the retiring President shouted me down with, "You are out of order!" Such interruption was rude, to put it mildly; but of course it is useless to proceed when people are not disposed to behave like gentlemen, so I retired gracefully. It appeared that a trap had been laid: a number of men had been brought from long distances to speak against the motion, and all were ready for disposing of the matter most effectually before the bulk of members had had time to comprehend the scope and bearing of the motion. The wrath of the disappointed faction is intelligible, as it still remains to bring it on next year, with this advantage to me, that the members did talk the matter over thoroughly, and all will be prepared on the side of the amendment as well as its opponents next year at Liverpool.

The address on Medicine was given by Dr. Wade, of Birmingham, in which he reviewed the progress of medicine since the foundation of the Association. He took the line of the improvement in practice caused by the progress of science, and that improved methods of observation required better mental training and a corresponding development of the mind. Not only was positive improvement so brought about, but great negative results followed in the avoidance of much that was harmful. In fact, he took a common-sense view of the present position of medicine.

Then came the great jubilee event of the meeting,—viz., the presentation of a bust of the late Sir Charles Hastings to the mayor and corporation of Worcester by the Association which he founded. This was done after a handsome collation given to the visitors by the Worcester and Hereford branch of the British Medical Association. When the memory of the founder was drunk, the toast was responded to by his son, Mr. Hastings. M.P. for the eastern division of the county. It was a handsome bust in marble by Mr. Brock, a Worcester artist. When Sir Charles Hastings died, a memorial fund was raised for a gold medal to be given annually by the Association for the best essay sent in on a given subject. It was awarded first to Dr. Thudichum, then to Furneaux Jordan, of Birmingham, then to Mr. Barker, of Bedford (dead), then to J. Milner Fothergill, and lastly to Lawson Tait, of Birmingham. The essays so rarely attained to the high-water mark required for the medal that the thing was abolished some years ago. The accumulations during the last few years were invested in the marble bust,—a very fitting use of it. (One of the other original founders of the Association was Dr. Malden, of Worcester, a man of much genial humor

as well as professional skill. A story is told of him that when the question of changing the fee from a guinea—a coin become obsolete—to a sovereign—the new coinage—was being discussed, the doctor took a way of his own of looking at the question. Holding betwixt finger and thumb a sovereign and a shilling, he said, "Mr. President, these coins were brought up together from their infancy, they have been associated in their youth, and now they must be considered as lovers," quoting from Thomson about Celadon and Amelia. "Hers"—the shilling—"the mild lustre of the blooming morn, and his"—the sovereign—"the radiance of the risen day. Mr. President, let no such lovers be parted." This touching allusion carried the day, and the proposed divorce betwixt the pound and the shilling was never pronounced. Had another decision been arrived at, the profession would have suffered a distinct and appreciable loss.) Hastings was a man of marked character, keen to observe and prompt to act. His mental operations were of such sound character that almost as soon as his student-life was concluded he was offered the chair of Physiology in his Alma Mater, the University of Edinburgh. Rejecting the brilliant career thus offered to him, he decided to settle in Worcester in practice. Even in those days the question of public health attracted his attention, and when the first outbreak of cholera occurred at Worcester he had the inhabitants of the poor neighborhoods, which bore the brunt of the scourge, removed outside of the town, where tents and booths were prepared for their reception. He saw the dead promptly buried, and their houses disinfected; indeed, he stood "betwixt the living and the dead," like the prophet of old. Not only was he a wise physician of advanced views, but he was no mean naturalist; and as a geologist, and the friend of Murchison and Sedgwick, he first pointed out the geological structure of the Malvern Hills, and of the salt-strata of the Droitwich salt-mines, the most important salt-industry in England, dating back to the Dark Ages. After this followed the Section meetings, where the serious work of the gathering goes on. In the Medicine Section, Clifford Allbutt, of Leeds, presided; in Surgery, Augustin Pritchard, of Bristol; in Obstetric Medicine, Prof. Leishman, of Glasgow; in Public Medicine, Alfred Carpenter, of Croydon; in Anatomy and Physiology, Prof. Humphry, of Cambridge; in Pathology, J. Hughlings Jackson; in Ophthalmology, Vose Solomases, of Birmingham; and in Otology, Laidlaw Purvis, of Guy's Hospital. Addresses were delivered by these gentlemen, and then the discussions proceeded.

The subjects mainly discussed were, the Treatment of Aggravated Hysteria and allied Neurasthenic Disease, in which Dr. Playfair took a leading part. A discussion on Diabetes also went on in the Pathology Section. In Surgery the great discussion was held on the Early Operative Treatment of Joint-Disease as a Preventive of Excision, in which many able surgeons took part. A lesser discussion went on on Bone-Setting. Subinvolution of the Uterus, its Causes, its Relation to Uterine Disease, and its Preventive Treatment, occupied much of the time of the Obstetric Section. In the Public Health Section the Alcoholic Question was brought forward by the irrepressible teetotaler, Norman Kerr; while the subject of the Notification of Infectious Disease was duly considered. Senile Cataract was ventilated in another Section; Auditory Vertigo, in another, and the Relation of Disease of the Ear to General Medicine. Papers of interest on other matters were also read. In the evening a grand oratorio was given in the cathedral, Worcester being famous for its musical festivals.

On Thursday morning work commenced by an address on Surgery by Prof. Stokes, of Dublin, the worthy son of an illustrious father. It is impossible to give any sketch of the address here: it was excellent in matter, well delivered, and listened to with the respectful admiration of a crowded audience. He paid a graceful tribute to Mr. Carden, of Worcester, who introduced the "single-flap" operation in amputation. He reviewed the present position of Listerism, and pointed out how surgery was hampered by the recent Vivisection Act. Then came more Sectional work; and, in the evening, the annual dinner of the Association, when Sir James Paget made the speech of the festive occasion, speaking with his usual silvery eloquence. On Friday morning came the first ominous rumble of a thunder-storm which it is promised shall break over the Association at its meeting next year in Liverpool, in the discussion on the compulsory notification of infectious disease by medical men, a matter to which I propose to devote my next letter; all the more important because in last week's number of the *British Medical Journal* appears a notice of a proposal, by Lewis Sayre, to have a Journal for the American Medical Association, in imitation of ours. Then followed the ceremonial formalities, the votes of thanks to each other for their self-denial, their unparalleled exertions, which courteously finish off the annual meetings as a matter of course. Soon all found their way to Madresfield Court, the seat of Earl Beauchamp, a "moated grange" under the shadow of the Malvern Hills. Here were beautiful grounds, along which the members of the Association, with their accompanying ladies, strolled to the sounds of sweet music, while a tent of ample dimensions offered fruit and cool drinks for those who wished them, and the heat and dust made such refreshments very grateful. In the evening was a *soirée*, where three times as many people were invited as Shire Hall would hold, to the crowding of all, visitors and natives alike.

Next morning the excursions drew off many of the members. Some went to Malvern, where a local archæologist discoursed of an old British camp on the top of one of the little peaks of the local Malvern group of hills, which seem formed by nature to serve as places for beacon-lights over a glorious plain. Others went to the river Wye, the beautiful western tributary of the Severn, alike attractive to sight-seers and anglers. A third party went eastward to Stratford-on-Avon, to see the humble home of Will. Shakspeare, now rescued from decay; on to the mighty home of the Earl of Warwick, the hero of the Wars of the Roses, towering over the Avon; to the more recent health resort, Leamington; and to the ruins of Kenilworth, where Amy Robsart pined till a mysterious accident was fatal to her, while Queen Bess occupied the mind and commanded the time of her husband, Robert Dudley. After this the meeting melted away, having visited all that Worcester could show them.

J. MILNER FOTHERGILL.

PROCEEDINGS OF SOCIETIES.

AMERICAN DERMATOLOGICAL ASSOCIATION.

THE Sixth Annual Congress of the American Dermatological Association, which has just finished its session at Newport, was very satisfactory as regards the attendance, and very successful as regards the number and high standing of the papers presented. It held two daily sessions on August 30 and 31, and one on September 1.

Dr. J. Nevins Hyde, of Chicago, President of the Association, besides delivering an annual address, read a paper on "Papillary Dermatitis of the Hairy Scalp," in which he reported several cases of a rare form of skin disease situated at the junction of the back of the neck and the scalp. The surface, though swollen, does not appear diseased, but the patch, which rarely exceeds the size of the palm of the hand, is distinctly circumscribed. Puncture of the part gives exit to a considerable quantity of pus, followed by a gummy fluid tinged with blood. The disease is non-parasitic, and appears to be due to an inflammation of the follicles of the skin at the part named.

Dr. C. Heitzmann, of New York, read two papers, one on "Myxo-Angioma of the Skin," and the other on "Ergot in some Forms of Skin Disease." The first referred to a very common vascular growth which contains new vessels and is therefore a true angioma. The superficial form also contains homogeneous substance, plastids, granular matter, etc., which the author regarded as myxomatous. The treatment advocated was extirpation with the scissors when the growths project, and the application of lunar caustic to the base, or smoking nitric acid applied directly, when the growth is sessile. Electrolysis was also recommended. In the second paper the use of ergot was highly commended in pruritus, acne, and some other forms of skin disease, given in half-drachm doses of the fluid extract several times a day.

Dr. Robert W. Taylor, of New York, read some "Notes on Psoriasis," in which he reported that he had traced in about one-fourth of his cases a syphilitic history in one or both parents, as had been suggested by Erasmus Wilson. He submitted the question for further investigation by members of the Association.

Dr. George A. Rohé, of Baltimore, reported two cases coming under his observation, where general psoriasis had followed vaccination with bovine virus.

Dr. Henry G. Piffard, of New York, in a paper on "Calx Sulphurates," endorsed the statement of Ringer that acne can be successfully treated with sulphide of calcium. He stated that the dose ordinarily should not be over one-eighth to one-sixth grain: he thought failures had occurred from giving it in too large doses. He also pointed out that the composition of the drug was very variable, and some specimens he had examined had contained little or none of real calcium sulphide, although dispensed for it by the druggists. He also had good success in the treatment of eczema in children and in non-specific sycosis in adults. As a remarkable fact, he had observed that in a diabetic patient the sugar completely disappeared while he was taking the remedy.

Dr. William A. Hardaway, of St. Louis, reported a curious case of pigmented neoplasm of the skin, and exhibited a full-sized painting of the patient, showing the appearance of the disease. It was not syphilitic, although the staining first appeared after large doses of iodide of potassium had been taken by the patient on his own responsibility.

Dr. A. R. Robinson presented a paper on "The Nerves of the Skin," illustrated by microscopic slides. Contrary to the usual belief, he showed that the nerves of the skin do not end in free ends, but form loops, and return into the superficial or deep plexus or into a neighboring papilla. The striated appearance of the tactile corpuscle he declared to be caused by a nervous plexus.

The question of the Contagion of Leprosy was reviewed by Dr. James C. White, who insisted that it was decidedly inoculable, and that sufficient danger of communication existed to warrant the attention of the National Board of Health to the possible dangers to the people of this country from this source.

Dr. I. E. Atkinson, of Baltimore, described a form of specific eruption which was called *syphiloderma papulosum circinatum*. This rare and peculiar cutaneous lesion, he said,

belongs to the early manifestations of syphilis. The spots affected are not formed by an aggregation of papules, as sometimes occurs in late syphilis, but are due to a single papular development which slowly enlarges at its border until it covers an area equal to a silver dollar, or larger, though rarely exceeding this size. The eruption may be sparse, and is then generally seen on the face and the neck, or it may be general, involving the entire body. Its course is slow. The lesions closely resemble ringworm, from which they are distinguished readily by their microscopic appearances; they have some features in common with erythema multiforme and with psoriasis, but attention to the history and the clinical characters will readily differentiate those distinct disorders.

A valuable tabulated report, based upon 58,617 cases of skin disease observed by members of the Association, was presented by Dr. White, Chairman of the Committee on Statistics.

A case of pellagra was reported by Dr. Sherwood, of the Long Island College Hospital.

The Association remained in session three days. Several new members were added at this meeting, and the following officers were elected: Dr. R. W. Taylor, of New York, President; Dr. I. E. Atkinson, of Baltimore, and A. R. Robinson, of New York, Vice-Presidents; Dr. A. Van Harlingen, of Philadelphia, Secretary; Dr. George H. Rohé, of Baltimore, Treasurer. The next place of meeting, Lake George; the time, the Wednesday nearest September 1, and the two following days.

REVIEWS AND BOOK NOTICES.

THE EXPERIMENTAL METHOD IN MEDICAL SCIENCE. By JOHN C. DALTON, M.D. Pp. 108. New York, G. P. Putnam's Sons, 1882.

This work comprises the second course of the Cartwright Lectures of the Alumni Association of the College of Physicians and Surgeons, New York, delivered during January and February of this year.

In these lectures the author has endeavored to furnish sketches which, while illustrating the manner in which some of our scientific knowledge in medicine has been obtained, will also serve to exhibit the close relationship between practical and scientific medicine, and the dependence of the permanent advancement of the one upon that of the other.

The first lecture is a sketch of "Galvani, and Galvanism in the Study of the Nervous System." The second is devoted to two quaint and obsolete doctrines which held a prominent place in physiology a century ago, and which were known as Buffon's "Theory of Organic Molecules," and Bonnet's "Theory of the Inclusion of Germs." The third, and last, is on the "Nervous Degeneration Theory of Sir Charles Bell."

This little work is carefully and entertainingly written, exhibits results of an evidently careful study, and, as a whole, is a task so thoroughly performed as to reflect much credit on its distinguished author and to deserve the thanks of the medical profession. It is a fitting companion to the recent writings on scientific medicine by Fothergill, Lauder Brunton, Bartholow, and others, and will occupy a merited position among the histories of medical science. E. T. R.

GLEANINGS FROM EXCHANGES.

TREATMENT OF PURULENT OTORRHŒA.—Dr. S. Pollak read a paper before the Medico-Chirurgical Society (*St. Louis Courier of Medicine* for May), in which he discusses the rational therapeutics in purulent otorrhœa, or perforating suppuration of the middle ear, which is timely and practical. We can give here only a few abstracts of this valuable communication. He says:

"From time immemorial *cleansing* of the ear with *water* was always considered the first step in the treatment of otorrhœa, and it is considered *absolutely indispensable* now. The auditory canal must be quite clean ere the first satisfactory examination can be made. The laws of general surgery obtain also in aural surgery.

"Foreign bodies, pus, fetid septic material, must be removed, whether from an open surface, from a cavity, or from a sinus. Wiping or swabbing with sponges, lint, oakum, or absorbent cotton will remove or absorb secretions, but *never cleanse*. . . .

"It is well known that death occurs, during many cases of otorrhœa, under pyæmic or septæmic symptoms, without *visible* caries of the petrous bone, or palpable alterations in the adjoining organs. It has been proved that schizophytes penetrate the walls of the lymphatics and of the blood-vessels in company with migratory cells, and cocci are swept into the circulation alone, or in company with thrombi, and thus cause metastasis in the lungs.

"With the abundant proof that schizomycetes colonize in the meatus in purulent perforative otorrhœa, the rational plan of treatment must necessarily be *antiseptic*, the aim of which is to destroy the putrefactive condition already present.

"Only in *acute* cases the *aseptic* treatment —*i.e.*, to *prevent* the immigration of the schizophytes, to stop the putrid decomposition of the secretion, as well as the suppuration—is indicated. Unfortunately, the opportunities are rare.

"In *acute disease* of *the middle ear—i.e.*, of the tympanal cavity, Eustachian tube, and

mastoid antrum and cells—we use the warm douche by siphon or fountain, or even the instilling of hot water with a spoon every few minutes; application of two or three leeches; inflation of the tube with either the Politzer air-bag or by the Valsalva method; paracentesis of the membrana tympani, not only to allay tension and pain and evacuate the accumulated fluids, but for the purpose of *disinfecting* the *tympanum*. Directly after the meatus is filled with finely-pulverized *boracic acid*, which is well borne, and fulfils the purpose of warding off the immigration of schizomycetes and causing rapid recovery, especially if confined to a warm room with perfect tranquillity of body. Opiates are not required, though a few drops of a solution of atropia (gr. $\frac{1}{100}$) instilled have often given prompt relief.

"In *chronic otorrhœa, antiseptics* are in order. The schizomycetes must be killed, or at least rendered innocuous, their immigration prevented, and the process of decomposition terminated. . . .

"But *antiseptic cleansing must be performed before any application can be made to the diseased surface.*

"The mere swabbing out of the meatus, the tympanum, and adjoining cavities with tampons of absorbent cotton *cannot* and *does not* cleanse. This can only be effected by *frequent syringing with a large amount of fluid and a forcible stream*, which will wash out the microbia and enfeeble the vitality of the micrococci which remain.

"*Superabundance* of moisture excites a noxious influence upon the growth of schizophytes, but a *slight* amount increases their growth.

"It is averred that by a great amount of fluid we run the risk of making the tissues swell too much by *excessive osmotic saturation*, which is a very serious objection, but which may be obviated by using *antiosmotic fluids*, such as a concentrated solution of *chloride of sodium* in *boiled* water.

"Common water always contains numerous micro-organisms, but boiling for a certain length of time destroys the propagative capacity of these structures.

"In order to avoid all possible danger of leaving decomposing material in the cavity, it is best to syringe abundantly and repeatedly with water which has been rendered antiseptic by *boracic acid*, and *alcohol*, which increases the antiseptic effect of boracic acid and exerts a beneficial and astringent action upon the diseased surface. At the same time air should be freely forced through the Eustachian tube by the Politzer air-bag or the Valsalva method of inflation; for stagnant air, like stagnant water, leads to putrid decomposition. Chloroform vapors may also be insufflated with advantage.

"The excellent effect of alcohol in suppurative otitis media by desiccation and molecular coagulation of albuminous fluids has long been known; its energetic action upon a diseased mucous membrane has always been recognized.

"We cannot lay too much stress upon the beneficial antiseptic action of alcohol. Its antiseptic effect is considerably increased by a combination with boracic acid. A liquid remedy can penetrate into all cavities and fissures, but it cannot *remain* in permanent contact with the diseased surface. This condition can be fulfilled by keeping a reserve of active material in the shape of a pulverized remedy, whose gradual solution produces a continued action.

"A supersaturated alcoholic solution of boracic acid, 10 to 20 per cent. more than the alcohol can dissolve, will meet this indication. This solution, slightly warmed and well agitated, is poured into the ear, and the boracic acid as carried along with the fluid reaches the entire surface. Let the solution remain in the ear as long as possible. Even granulations and polypi disappear under this treatment without direct operative interference.

"Insufflation of *dry* boracic acid, as advocated by Bezold, does not meet the requirement. It is, in the first place, coarsely triturated, and causes traumatic irritation; and, secondly, it is not easily soluble in water, and it is apt to concrete in the cavity and to occlude it entirely. I remember having had under treatment a lad aged eight years, a victim of perforating suppuration of the middle ear; the discharge was very abundant and fetid, so that he had to leave school. I determined to try the entire dry antiseptic treatment without *previous* syringing. I dipped the absorbent cotton probe in again and again without being able to remove the entire fluid contents of the cavity, and still less to correct the fetor. I had to resort to the syringe at last. The cavity was promptly cleansed, deodorized, and dried. I insufflated finely-pulverized boracic acid, so that the entire mucous surface of the cavity was covered with it, and I filled the whole meatus with it besides. In three days the boy returned, feeling very uncomfortable, complaining of pain and vertigo. The meatus was hermetically closed, as if filled with cement. The probe made no impression upon the concretion. Water would not soften it, but alcohol gradually did, so that I could drill and scoop it out and give exit to a large accumulation of fluid. The relief was instantaneous. I cleansed the ear again with the syringe, but substituted the borate of sodium for the boracic acid, filling the meatus with it to the brim. Next morning not a trace of it was left; it had entirely dissolved. I suggested to the parents to syringe the ear with boiled water and a little common salt, and fill the ear with borate of sodium, whenever a discharge was visible. The result was satisfactory; fetor disappeared entirely, the discharge lessened and gradually ceased; but

the perforation in the membrana tympani is as large as ever. H. D. 24 inches. Politzer uses sulph. of alum for insufflation, but parasites have been found (*aspergillus penicilium*) in a solution of alum; it is known they cause otomycosis. The burnt alum may do better.

"The absolutely *dry method* of *treatment* of otitis media purulenta has come in vogue only of late, and has found two able advocates in this city, whose opinions are entitled to the highest respect. I cannot learn that this plan has found favor elsewhere. With all due deference to our *home* aurists, I am constrained to dissent from their views. They cannot stand the light of investigation, are impractical in their application, and unsupported by authority and experience.

"Although insufflation of dry remedies is as often practised as instillation of lotions, it should only be done *after* cleansing the ear with water and syringe. My reasons for not favoring the exclusive dry treatment, for not preferring the cotton probe to the syringe, are:

"None but aurists are likely to be provided with the appliances of aural surgery. The use of the mirror, speculum, and probe requires good light, good sight, great manual dexterity, and docile, reasonable, and obedient patients. Children, nervous people, are timid, restive, and resisting. Of course all proceedings are then ended. But a mere tyro can use the syringe. Parents and nurses can be easily instructed how and when to use the syringe, or they can be limited to the mere pouring in of boiled water with salt and letting it run out again.

"They can be taught insufflation as easily as instillation, which cannot be done too often. For when there is fetor there is decomposition, there is sepsis, and there are micro-organisms, which must be at once and very energetically treated by cleansing and antiseptics, whether with dry borax by insufflation or a supersaturated alcoholic solution of boracic acid.

"It is not probable that patients will visit aurists whenever they perceive a little fetid discharge; and yet it must be promptly and vigorously met.

"We are bound to rely on nurses in most cases of sickness, but in none more so than in this. The aurist can hardly do much more or better, except when the absolute dry treatment, without previous proper cleansing, is determined upon. The probing can only be done by the well-trained aurist. But the most skilful manipulation of the cotton probe is more irritating than the syringing, and at no time as efficient. No amount of wiping, even to dryness, can remove fetor. By aspirating, Politzerizing, or Valsalving, ventilation of the drum cavity may be effected, stagnant air and excess of fluid may be expelled, but the surface remains moist and continues to be the breeding-place for parasites. But even ventilation may not always be feasible; the tube may be impervious; and with children it is only accidentally effective.

"Iodoform has been much recommended in suppurative inflammation of the middle ear, but was abandoned after a fair trial. Its pungent odor was insufferable both to the patients and their surroundings, and could not be disguised. It was even tasted for hours after insufflation. The syringing and antiseptic treatment with either lotion or powders finds application in all cases. A judicious use of constitutional remedies should not be neglected in otological practice. Considering that purulent otorrhœa is occasionally a sequel of syphilis, of rheumatism, of struma, it is evident that a diathesis of these diseases must be met with a treatment indicated in these cases.

"As in ophthalmic practice, so in otological, internal treatment has proved of inestimable value.

"*Mercury* occupies the front rank. Sir William Wilde says, 'It is the remedy which of all others acts most beneficially and with specific efficacy in diseases of the ear.' This strong and unqualified praise, though not shared by *most* modern authorities, is yet endorsed by a good many. I have obtained most gratifying results from a persistent use of the bichloride and biniodide of mercury in doses of from $\frac{1}{48}$ to $\frac{1}{8}$ of a grain three times a day, and even then when there was not the least taint of syphilis discernible or suspected. In my hospital record a stereotype formula of the biniodide is very often found, both in eye and ear cases. Especially was it found of great advantage when the tympanal inflammation was threatened with or gave rise to intracranial complication. Periostitis of the tympanum will soon be followed by periostitis of the antrum and mastoid cells, and of the dura mater.

"Muriate of ammonia, pyrophosphate of soda, sulphide of calcium, pulsatilla, have been recently spoken of, but I have not tried them sufficiently to have an opinion about them.

"I am, however, convinced of the great value of tonics in chronic aural diseases with discharges, especially the quinine, iron, and strychnia.

"Most of the distressing symptoms in aural diseases are more or less amenable to local and constitutional treatment, with the exception, perhaps, of *tinnitus aurium*, as an objective symptom. I have yet to learn the remedy which in some cases has given the least relief, though I went through the whole list. I know of cases who went from aurist to aurist in this country and in Europe, and were brought to the verge of insanity, without obtaining the least relief.

"The allusion to constitutional treatment will get no response from specialists,—*i.e.*, who are specialists *only*,—but will readily be accorded in by the profession at large. The

eminent ophthalmic and aural surgeon, Dr. Theobald, in one of his lectures on the use of constitutional remedies in the treatment of ear diseases, very aptly says, 'The mere specialist in otology *overestimates* the value of purely local measures, and *underestimates* the value of constitutional remedies.'

"Only by a judicious and intelligent combination of both may great results be achieved."

ESTIMATION OF QUINIA.—After a consideration of various methods of assaying cinchona bark (*Ephemeris*, vol. i. No. 4), Dr. E. R. Squibb makes the following remarks with regard to the mode of estimation of quinia:

"After much labor extended over many years, and the trial of all the principal processes which have been published, the writer is obliged to acknowledge that he has found no process for the accurate separation of the cinchona alkaloids which was within the scope of his ability to apply with success. The more complicated and delicate processes of the higher chemists seem only successful in their hands, or at least none of them have thus far come into any general use, and under these circumstances it seems only practicable, in a general way, to reach near approximations by some method which is simple and easy of application.

"This much only is claimed for the following process:

"It is common to have the cinchona alkaloids divided into ether-soluble alkaloids and those not soluble in ether. But this is a very inaccurate subdivision, for all are quite soluble in ether whether the ether be absolute or 94 per cent., and the application of ether to any mixture will easily dissolve the whole. Thus either the powdered bark itself, or after having been mixed with milk of lime and dried, can easily be exhausted of alkaloids by ether alone. All that can be said is that quinia, quinidia, and cinchonidia are more soluble in ether than the other alkaloids, and that quinia is most soluble of all, and is very soluble,—so soluble that it dissolves in large quantity in ether that has been already saturated with other less soluble alkaloids. And, further, that in the presence of any ordinary proportion of any or all the other cinchona alkaloids all the quinia of a mixture will be dissolved by ether if enough of this solvent be present to fully dissolve the quinia if that alkaloid was alone. It is, however, still useful to distinguish the more valuable cinchona alkaloids, namely, quinia, quinidia, and cinchonidia, as the ether-soluble alkaloids, because they can be roughly but still usefully separated by ether in such a way as to better define the values of various barks as they come into the markets for use, and the following process has been contrived to give a fairly good account of the so-called ether-soluble alkaloids as a group, if all are present, and a somewhat less definite account of the quinia as well.

"Into the flask containing the total alkaloids, after these have been weighed, put first 5 grammes = 78 grains of glass which has been ground up in a mortar to a mixture of coarse and fine powder, and then 5 c.c. = 80 minims of stronger ether. Cork the flask and shake it vigorously until by means of the glass all the alkaloids have been detached from the flask and ground up in the presence of the ether into fine particles. In this way the definite quantity of ether, which is large enough to dissolve all the quinia that could possibly be present, becomes entirely saturated with alkaloids in the proportion of their solubility, and the solution will necessarily embrace all the very soluble ones as the quinia.

"Next, mark two test-tubes at the capacity of 10 c.c. = 160 minims each, and place a funnel and filter of 7 c.m. = 2.8 inches diameter over one of them. Wet the filter well with ether, and then pour on to it the mixture of alkaloids, ether, and glass, from the flask. Rinse the flask out two or three times into the filter with fresh ether, and then wash the filter, and percolate the glass with fresh ether, applied drop by drop from a pipette, until the liquid in the test-tube reaches the 10 c.c. = 160 minim mark. Then change the funnel to the other test-tube, and continue the washing and percolation with ether until the mark on the second test-tube is reached by the filtrate. Pour the contents of the two test-tubes into two small tarred capsules, evaporate to a constant weight, and weigh them. The first capsule will contain what may be called the ether-soluble alkaloids. Subtract from the weight of these the weight of the residue in the second capsule, and the remainder will be the approximate weight of the quinia extracted from the 5 grammes of bark. These weights multiplied by 20 will give the percentage of ether-soluble alkaloids and of quinia.

"The explanation upon which these conclusions are based is as follows:

"The quantity of ether used is abundant to dissolve all the quinia and most of the quinidia and cinchonidia, and presumably does so, and dissolves, besides, all that it is capable of holding of the less soluble alkaloids. This saturated solution is filtered off, displaced, and washed out. Then an equal volume of the solvent ether is applied to the residue containing the less soluble alkaloids, and is presumably nearly saturated by these, but contains no quinia, and but little quinidia perhaps, though it contains as much of all the other alkaloids as did the first portion. If the two equal volumes of solvent, then, contain nearly equal quantities of the less soluble alkaloids, while the first contains nearly all of the more soluble ones, then it only needs that the weight of the second residue be subtracted from the weight of the first

to leave only the weight of the more soluble alkaloids, such as quinia and quinidia if the latter should be present.

"In two good critical assays, one of red and the other of yellow cinchona, made for the purposes of this paper at this time, the red cinchona (succirubra of Ceylon) gave .335 grammes of total alkaloids, which is (.335 × 20) = 6.7 per cent. These total alkaloids then gave .210 grammes of ether-soluble alkaloids, which is equal to (.210 × 20 =) 4.2 per cent., and this corrected by subtracting .015 grammes of less soluble alkaloids, or (.015 × 20 =) .3 per cent., gives (4.2 — .3 =) 3.9 per cent. of quinia. Then, as the ordinary sulphate of quinia contains about 73.5 per cent. of quinia, this 3.9 per cent. of quinia would be equal to (as 73.5 : 100 :: 3.9 :) 5.3 per cent. of sulphate.

"The yellow bark assayed at the same time (Cinchona officinalis from the *Ootacamund*) gave of total alkaloids 7.3 per cent. Ether-soluble alkaloids 3.48 per cent. Quinia 2.76 per cent. Equal to sulphate of quinia 3.75 per cent.

"In connection with these two assays it is worthy of remark that here, as is very rarely the case in the experience of this writer, the red cinchona yields the smaller percentage of total alkaloids with the larger percentage of quinia. Usually the proportions are just the reverse of this between the red and yellow barks."

REMOVAL OF THE UTERINE APPENDAGES.—At the July meeting of the Obstetrical Society of London, Mr. Lawson Tait showed fifteen specimens of uterine appendages removed by him since December, 1881, for hydro- or pyo-salpinx. The symptoms were pain aggravated by walking, by marital intercourse, and at the menstrual period. Five cases were due to gonorrhœa, and four either due to or aggravated by pessaries. In most, the operation gave immediate and complete relief. In all there was improvement: none had died. He objected to the terms "spaying," "castration of women," "normal ovariotomy," because they implied that healthy ovaries were removed, an operation which he had never done. He thought the operation of doubtful value in neurasthenic cases. Of these he had only done four, and at present was not disposed to go further. For myoma, its mortality was less than that of lithotrity in the male, and its results were more certain. For the class of cases from which the specimens exhibited were taken, it was the only means which offered a hope of relief.—*British Medical Journal.*

LEPROSY TREATED WITH CHAULMOOGRA OIL.—A case of incipient true Eastern leprosy was treated by Dr. Startin, of London, with three capsules of Chaulmoogra oil daily, with inunctions of the crude oil, with decided amelioration of the symptoms.—*Lancet*, July 29.

NOTES AND QUERIES.

PHILADELPHIA COUNTY MEDICAL SOCIETY LECTURES.

PROF. AUSTIN FLINT, Senior, of New York, has accepted the invitation to deliver the series of 1882-83. His course will consider practical points in the physical diagnosis of visceral lesions.

AT a recent meeting of the Council, the annual meeting of the American Academy of Medicine was postponed until Thursday, October 26, when it will take place at Philadelphia at the time of the Bi-centennial Celebration.

OFFICIAL LIST

OF CHANGES OF STATIONS AND DUTIES OF OFFICERS OF THE MEDICAL DEPARTMENT U.S. ARMY FROM AUGUST 18 TO SEPTEMBER 1, 1882.

MURRAY, ROBERT, COLONEL AND SURGEON.—Relieved from duty as Medical Director, Military Division of the Missouri, and to report in person to the Commanding General, Military Division of the Atlantic and Department of the East, for duty as Medical Director of that division and department. S. O. 191, A. G. O., August 18, 1882.

BROWN, J. B., LIEUTENANT-COLONEL AND SURGEON.—Granted leave of absence for six months on surgeon's certificate of disability. S. O. 200, A. G. O., August 29, 1882.

BILL, J. H., MAJOR AND SURGEON.—Granted leave of absence to December 1, 1882. S. O. 196, A. G. O., August 24, 1882.

ALDEN, CHARLES H., MAJOR AND SURGEON.—Granted leave of absence for three months. S. O. 196, c. s., A. G. O.

SMITH, A. K., MAJOR AND SURGEON.—Granted leave of absence for one month on surgeon's certificate of disability. S. O. 131, Department of Arizona, August 22, 1882.

HUBBARD, V. B, MAJOR AND SURGEON.—Assigned to duty at Fort Wingate, N.M. S. O. 172, Department of the Missouri, August 28, 1882.

MUNN, C. E., CAPTAIN AND ASSISTANT-SURGEON.—The leave of absence granted him in S. O. 147, July 28, 1882, Department of the Missouri, is extended two months. S. O. 196, c. s., A. G. O.

SKINNER, J. O., CAPTAIN AND ASSISTANT-SURGEON.—To take charge of Medical Director's office, Department of Arizona. S. O. 131, Department of Arizona, August 22, 1882.

SPENCER, WM. G., CAPTAIN AND ASSISTANT-SURGEON.—The leave of absence granted him in S. O. 80, April 7, 1882, from A. G. O., is extended two months. S. O. 191, c. s., A. G. O.

BARROWS, CHARLES C., ASSISTANT-SURGEON.—Assigned to duty at Fort Grant, A.T. S. O. 130, Department of Arizona, August 21, 1882.

OWEN, JR., WM. O., FIRST-LIEUTENANT AND ASSISTANT-SURGEON.—Assigned to temporary duty at Vancouver Barracks, W.T. S. O. 114, Department of the Columbia, August 11, 1882.

EGAN, P. R., ASSISTANT-SURGEON.—Assigned to duty at Fort Bowie, A.T. S. O. 134, Department of Arizona, August 25, 1882.

WAKEMAN, W. J., FIRST-LIEUTENANT AND ASSISTANT-SURGEON.—Now at Omaha, Nebraska; to report to the Commanding Officer, Fort D. A. Russell, Wyoming, for duty. S. O. 88, Department of the Platte, August 25, 1882.

MACAULEY, C. N. B., FIRST-LIEUTENANT AND ASSISTANT-SURGEON.—Assigned to temporary duty at Fort Columbus, N.Y. S. O. 147, Department of the East, August 25, 1882.

MACAULEY, C. N. B., FIRST-LIEUTENANT AND ASSISTANT-SURGEON.—To report in person to the Commanding General, Department of the East, for assignment to temporary duty. S. O. 192, A. G. O., August 19, 1882.